MEDICAL LIBRARY
Med. Library
MEDICAL LIBRARY
SEP 7 '48

Official Journal of the
INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

MEDICAL LIBRARY

VOLUME 4, Number 2 AUGUST 1948

ASTRIC ACHLORHYDRIA AND SUBACUTE OMBINED DEGENERATION OF HE SPINAL CORD
Tom D. Spies, M.D., ET AL.

MALL, COMMONLY UNRECOGNIZED STROKES
Walter C. Alvarez, M.D.

HE CLIMACTERIC IN WOMEN AND MEN
August A. Werner, M.D.

HE TREATMENT OF PROSTATIC CANCER
Reed M. Nesbit, M.D.

HE PRESENT STATUS OF ANTIBIOTIC THERAPY
John A. Kolmer, M.D.

Diagnostic Clinics

SURGERY OF THE PANCREAS
Richard B. Cattell, M.D.

DIAGNOSIS AND TREATMENT OF HYDRONEPHROSIS
Herman L. Kretschmer, M.D.

THE FARMER'S BACK
Robert D. Schrock, M.D.

BENIGN PROSTATIC HYPERTROPHY AND NEUROGENIC BLADDERS
Dalton K. Rose, M.D.

THE RESULTS OF ELECTRIC SHOCK THERAPY
Leland B. Alford, M.D.

Complete Table of Contents on Page 5

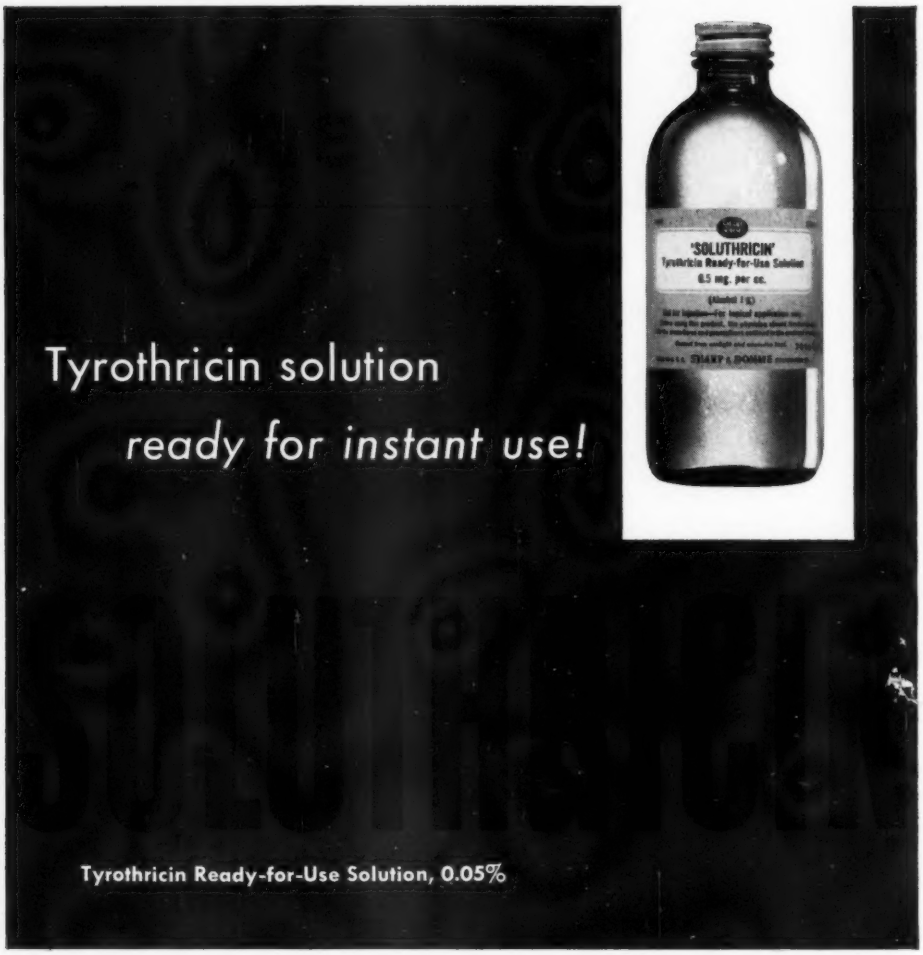
ternational Assembly — Public Auditorium, Cleveland, Ohio, November 9 to 12, 1948, 33rd Year.

From the Mayo Clinic — August Surgical Clinics of North America

HYMAN'S INTEGRATED PRACTICE OF MEDICINE

Complete Details in Saunders Advertisement on Pages 6 and 7

(Advertisement)



Development of special laboratory methods by Sharp & Dohme's Medical Research Division has produced a new, *solubilized* form of tyrothricin ready for immediate use, *sterile* at time of initial application, *clear* in appearance, *stable* at room temperature for more than one year, flocculation and precipitation proof, *ideal* for prescription compounding.

SOLUTHRICIN Solution contains 0.5 mg. of *solubilized* tyrothricin per cc. (0.05%).

It is approximately isotonic with blood serum, and has a surface tension of about 40 dynes per cubic centimeter.

SOLUTHRICIN Solution is for topical use only and is administered by irrigation, wet dressing, drops, spray, or by instillation in body cavities not connected with the blood stream.

SOLUTHRICIN Solution is indicated in treatment of external ulcers, abscesses of the skin and soft tissues, chronic purulent otitis media, mastoiditis, acute sinusitis, osteomyelitis, empyema, and many types of wound and ophthalmic infections. SOLUTHRICIN Solution is supplied in 240-cc. bottles, 0.5 mg. of *solubilized* tyrothricin per cubic centimeter. Sharp & Dohme, Philadelphia 1, Pa.

POSTGRADUATE MEDICINE

OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA -- ORGANIZED IN 1915

AUGUST, 1948 — VOL. IV, No. 11

Table of Contents

Special Articles

THE ASSOCIATION BETWEEN GASTRIC ACHLORHYDRIA AND SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD.
Tom D. Spies, M.D., ET AL. 89

SMALL, COMMONLY UNRECOGNIZED STROKES.
Walter C. Alvarez, M.D. 96

THE CLIMACTERIC IN WOMEN AND MEN.
August A. Werner, M.D. 102

THE TREATMENT OF PROSTATIC CANCER.
Reed M. Nesbit, M.D. 111

THE PRESENT STATUS OF ANTIBIOTIC THERAPY.
John A. Kolmer, M.D. 115

Diagnostic Clinics

SURGERY OF THE PANCREAS.
Richard B. Cattell, M.D. 121

THE DIAGNOSIS AND TREATMENT OF HYDRONEPHROSIS.
Herman L. Kretschmer, M.D. 129

THE FARMER'S BACK.
Robert D. Schrock, M.D. 132

DIFFERENTIAL DIAGNOSIS, BENIGN PROSTATIC HYPERTROPHY, AND NEUROGENIC BLADDERS.
Dalton K. Rose, M.D. 140

THE RESULTS OF ELECTRIC SHOCK THERAPY.
Leland B. Alford, M.D. 149

Scientific Exhibit

GLOMERULAR NEPHRITIS; RECOGNITION AND TREATMENT.
Fred I. Gilbert, Jr., M.D., and L. Martin Griffin, Jr., M.D. 153

Departments

THE MEDICAL BOOKMAN. *Physical Medicine in General Practice* 161
MEN OF MEDICINE. *Frank Howard Lahey, M.D.* 166
A PORTRAIT HISTORY OF CARDIOLOGY. *Murals by Diego Rivera* 175
EDITORIALS. *American Specialty Board Certification • Medical Aspects of Anxiety* 177
NEW DRUGS 180
MEDICINE MAKES NEWS 183
LEAVES FROM A DOCTOR'S DIARY 184

Saunders

From the MAYO CLINIC

August Surgical Clinics of North America

with a SYMPOSIUM on SURGICAL PHYSIOLOGY and 13 OTHER HELPFUL CLINICS

The SYMPOSIUM on SURGICAL PHYSIOLOGY

Apparatus for Recording Physiologic Variables During Operations on Man, With Observations on Changes of Blood Pressure During Resection for Coarctation of the Aorta—By Drs. George A. Hallenbeck, Earl H. Wood and C. Theron Clagett.

Surgical Treatment of Imbalance of Extraocular Muscles: Physiologic Aspects—By Dr. Avery deH. Prangen.

Physiologic Disturbances Underlying Development of Early Postoperative Atelectasis After Lobectomy—By Dr. William D. Seybold.

Surgical Treatment of Congenital Megacolon—By Drs. Claude F. Dixon and David B. Judd.

Jejuno-ileac Insufficiency: It's Relation to the Sprue Syndrome—By Drs. E. Leonard Posey, Jr. and J. Arnold Bargen.

Care and Prevention of Decubitus Ulcers—By Dr. Elwyn S. Shonyo.

CLINICS on OTHER SUBJECTS

Eosinophilic Granuloma of the Skull—By Drs. George S. Baker and Robert G. Fisher.

Volvulus of the Cecum—By Drs. Claude F. Dixon and Alfred C. Meyer.

Diagnosis in Foot Pain—By Dr. Mark B. Coventry.

Traumatic Paralysis of Sciatic Nerve Associated With Fracture of Rim of the Acetabulum and Dislocation of the Hip—By Dr. Henry W. Meyerding.

Gangrenous Cholecystitis—By Drs. Leonard C. Hallendorf, Malcolm B. Dockerty and John M. Waugh.

Acute Pseudomembranous Enteritis or Enterocolitis—By Drs. Claude F. Dixon and Rodger E. Weismann.

Aseptic Necrosis of the Head of the Femur Following A Minor Fracture of the Greater Trochanter—By Drs. Alfred E. Jackson and William H. Bickel.

Epidermoid Cyst of the Left Palm with Dupuytren's Contracture of the Hands and Right Foot—By Drs. Henry W. Meyerding and Alfred E. Jackson.

Pyloric Stenosis Caused by Ingestion of Corrosive Substances—By Drs. Howard K. Gray and Chester L. Holmes.

Association of Carcinoma of Thyroid Gland and Exophthalmic Goiter—By Drs. John deJ. Pemberton and B. Marden Black.

Urographic Findings in Cases of Tumor of the Suprarenal Gland—By Drs. Joseph H. Kaplan and Laurence F. Greene.

Postgastrectomy Gastritis—By Drs. Howard K. Gray, Ward C. Meyers and Malcolm B. Dockerty.

Malignant Tumors of Glandular Nature Found in the Nose, Throat and Mouth—By Drs. John R. McDonald and Fred Z. Havens.

The Surgical Clinics of North America. Issued serially, one number of about 250 pages, 6" x 9", illustrated, every other month. Per year (six consecutive bimonthly numbers): Cloth Binding, $18.00; Paper Binding, $15.00. Sold only by a year of six consecutive numbers.

Published by Saunders—USE THIS FORM TO ORDER ⟶

The Association Between Gastric Achlorhydria and Subacute Combined Degeneration of the Spinal Cord

TOM D. SPIES,[1] ROBERT E. STONE,[2] GUILLERMO GARCIA LOPEZ,[3] FERNANDO MILANES,[4] TOMAS ARAMBURU,[5] AND RUBEN LOPEZ TOCA[6]

NORTHWESTERN UNIVERSITY, CHICAGO, AND UNIVERSITY OF HAVANA, CUBA

It has long been recognized that persons with pernicious anemia have an imperfect secretion of gastric juice. As early as 1870, Fenwick[1] stressed the possibility of an important relationship between the gastric secretions and blood formation. Castle and his associates[2] have done a great deal to establish experimentally the nature of the abnormality in gastric function and the anti-anemic substances stored in the liver. The cause of the gastric dysfunction *per se,* however, is not elucidated. Pernicious anemia often occurs in several members of a family and frequently in succeeding generations, but whether this dysfunction is congenital or is an acquired defect has not been conclusively settled. The disease usually occurs late in life.

[1]Professor of Nutrition and Metabolism and Chairman of the Department, Northwestern University, Chicago, Illinois.
[2]Associate Director, Nutrition Clinic, Birmingham, Alabama.
[3]Associate Professor of General Pathology, University of Havana, Havana, Cuba.
[4]Associate Professor of General Pathology, University of Havana, Havana, Cuba.
[5]Williams-Waterman Fellow in Nutrition.
[6]Rockefeller Fellow in Nutrition.
This study was supported by a grant from Lederle Laboratories, Inc.
Northwestern University Studies in Nutrition at the Hillman Hospital, Birmingham, Alabama, and at the Calixto Garcia Hospital, Havana, Cuba.
From the Department of Nutrition and Metabolism, Northwestern University and the Department of General Pathology, University of Havana.

Whatever may be the pathogenesis of the anemia and the gastric dysfunction, it has long been recognized that there is an association between neural degeneration and pernicious anemia. Leichtenstern[3] in 1884 published an account of 3 patients with pernicious anemia in whom "tabes dorsalis" was present. In 1893 Nonne[4] discussed the association of neural degeneration and pernicious anemia. Recently, Rundles[5] has reviewed the more modern aspects of subacute combined degeneration. The anemia usually precedes the neural disturbances although neural disturbances may occur without any blood changes and it is well known that the extent of the neural involvement is not directly dependent on the degree of anemia present.

In recent years it has become increasingly clear that there are a number of types of macrocytic anemia that will respond to liver extract. It now has become widely accepted that folic acid is an anti-anemic factor which stimulates the bone marrow of persons with Addisonian pernicious anemia, nutritional macrocytic anemia, and the macrocytic anemia of pellagra, pregnancy, and sprue.[6] It is abundantly clear that folic acid neither prevents subacute combined degeneration nor cures it once it has developed.[6-11] The present study, which has ex-

TOM D. SPIES

tended over two years, is concerned with efforts to determine in advance the susceptibility to subacute degeneration of the spinal cord in persons with macrocytic anemia and with gastric achlorhydria in contrast to persons with macrocytic anemia without gastric achlorhydria, once they are started on folic acid therapy.

MATERIAL AND METHODS

One hundred and sixty adult patients* with macrocytic anemia were selected in Birmingham, Alabama, and in Havana, Cuba, using the following basic criteria: (a) a color index of 1 or more; (b) a red blood cell count of 2,500,000 or less; (c) megaloblastic arrest of the sternal bone marrow; (d) the patient must be untreated or not have been treated recently enough to interfere with the evaluation of antianemic therapy; and (e) the patient must have no evidence of subacute combined degeneration of the spinal cord.

These patients were then classified as to the type of anemia. Group 1 included 37 cases in Birmingham and 1 case in Havana who had a histamine refractory achlorhydria on repeated gastric analyses† who were tentatively diagnosed as Addisonian pernicious anemia. (Not included in this series were 4 other patients in the Havana group who had no free hydrochloric acid in the gastric contents after histamine stimulation. These patients had acid steatorrhea and a long history of "sprue-like" symptoms. They responded promptly and fully to folic acid and are now in good health and will not be discussed further in this report.)

Group 2 included 13 cases in Birmingham and 18 in Havana who had free hydrochloric acid in the gastric secretions after histamine stimulation and evidence of concomitant nutritive failure, who were tentatively diagnosed as nutritional macrocytic anemia. (We see a relatively small number of patients with nutritional macrocytic anemia and sprue who have no free acid after histamine stimulation who change after treatment and have free acid, but this is not usually the case.)

Group 3 included 5 pregnant women in Havana who had typical macrocytic anemia without other complications who were diagnosed as the macrocytic anemia of pregnancy.

Group 4 included 82 patients in Havana who were diagnosed as having tropical sprue. These patients had free hydrochloric acid and enzymes in the gastric secretion after histamine stimulation; a flat curve after a single oral dose of glucose; glossitis; diarrhea characterized by steatorrhea, and a weight loss of at least 30 pounds in the six months prior to study.

The patients were admitted to the hospital where rigid dietary control was initiated and was maintained throughout the course of the

*Four patients with aleukemic leukemia, 3 with aplastic anemia, and 4 who could not be classified to the satisfaction of all observers were not included in this series although they were studied intensively.

†We have found, as have many others, that some 20 per cent of the patients in the older age groups have no free hydrochloric acid in the gastric secretions after histamine stimulation but do not have anemia. Occasionally patients with histamine refractory achlorhydria developed free hydrochloric acid after treatment. Accordingly, we make only a tentative diagnosis of pernicious anemia based on the absence of free hydrochloric acid in the gastric secretions.

study. Meat, meat products, fish, poultry, milk, cheese, and eggs were excluded from the diets.

Hematologic examinations were made daily with the assistance of Mary B. Koch, Margaret H. Caldwell, Virginia Minnich, Jane Davis, Georgia Gwinner, Belle Culver, Madeline Hill, Mary Sax, Ann English, Doris Godwin, Helen Grant, and Anne Ellis. The laboratory determinations included white cell and erythrocyte counts, hemoglobin determinations, and reticulocyte counts daily. The hemoglobin content of the blood was determined in grams by means of a Leitz photoelectric colorimeter. The reticulocytes were counted in wet preparations by the use of a modified brilliant blue solution of Dameshek. Permanent fixed preparations of blood smears were made on all patients on admission and just prior to therapy and, once or twice a week thereafter, cell volumes were determined on oxalated venous blood by means of Wintrobe hematocrit tubes.

In each case, bone marrow was obtained prior to treatment by sternal aspiration using a Turkel trephine instrument for biopsies and marrow infusions—14-17 gauge, 20 mm. long. An effort was made to obtain another specimen at the peak of reticulocytosis, and still another was obtained when the reticulocytes returned to normal. Differential counts were made on preparations with both supravital and Wright-Giemsa stains. Icteric index was determined on those patients whose skin had a lemon-yellow color.

Repeated gastric analyses were performed by Dr. Aureliano Rodriguez in Havana and by Monette Springer, Alice Rogers, Frances Prudich, and Jean Brandenburg in Birmingham. The gastric contents were tested for hydrochloric acid using Toepfer's reagent. In a few special cases the presence or absence of the intrinsic factor was determined by the method of Castle on subjects known to have pernicious anemia.

Roentgenologic examinations of the gastrointestinal tract were performed on the cases in Havana by Dr. R. L. Hernandez Beguerie and on the cases in Birmingham by the staff of the Department of Radiology, Medical College of Alabama. Samples of the stools of most of the patients with tropical sprue were studied for ova, parasites, pathogenic bacteria and occult blood, and for fat by Drs. Fernando Milanes, Arturo Curbelo, Aureliano Rodriguez, and Pedro Kouri.

Folic acid was administered to each patient orally after all the baseline determinations were made. The dosage varied from 10 to 50 mg. daily but the great majority of patients received 10 mg. daily.

OBSERVATIONS

There was a prompt hematologic response following the administration of folic acid in each of the cases included in the study. A remarkable clinical improvement paralleled the hematologic response. Each patient volunteered that he felt much stronger than he had for a long time and that the desire for food had returned. Patients who, prior to treatment, had no desire to move, began to walk about. They began eating all the food offered on the experimental diet and frequently asked for additional servings. In all the patients who had lost weight there was a prompt gain in weight. The typical hematologic response, increase in food intake, and weight gain is shown in Figure 1, both during therapy and for several months thereafter.

WITHIN two years, but usually within a few months, 27 of the 37 cases in Birmingham and the single case in Havana diagnosed as pernicious anemia developed subacute combined degeneration. Each of these patients had prompt relief from the neural disturbances following the administration of liver extract. In contrast, no evidence of subacute combined degeneration developed in any of the 13 patients in Birmingham or the 18 in Havana diagnosed as having nutritional macrocytic anemia, or in the 5 patients diagnosed as the macrocytic anemia of pregnancy and the 82 diagnosed as tropical sprue in Havana, despite the fact that

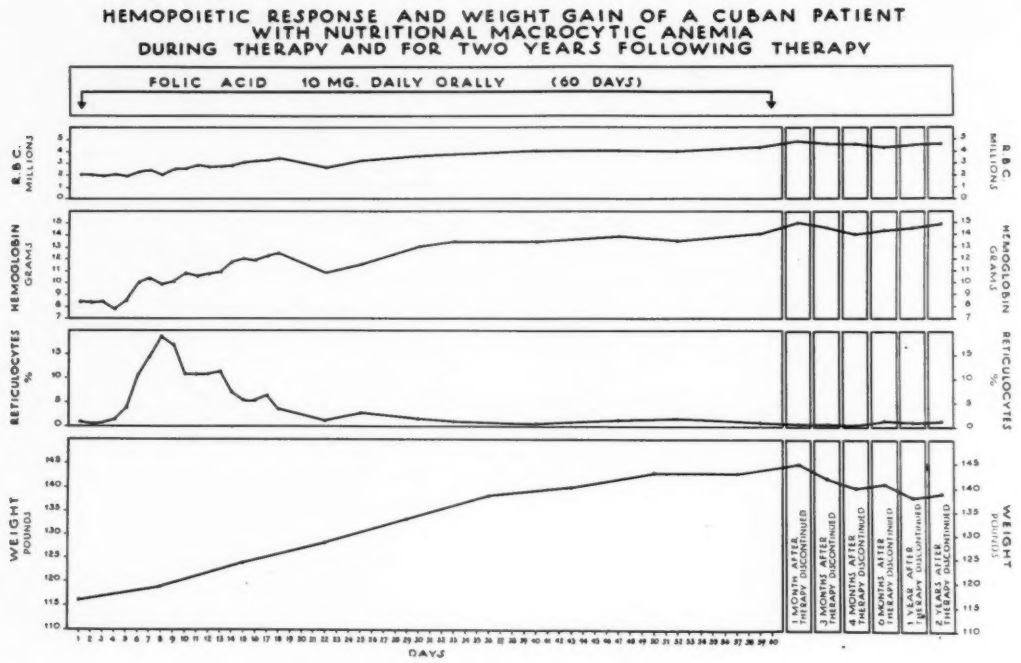

HEMOPOIETIC RESPONSE AND WEIGHT GAIN OF A CUBAN PATIENT
WITH NUTRITIONAL MACROCYTIC ANEMIA
DURING THERAPY AND FOR TWO YEARS FOLLOWING THERAPY
FOLIC ACID 10 MG. DAILY ORALLY (60 DAYS)
R.B.C. MILLIONS
HEMOGLOBIN GRAMS
RETICULOCYTES %
WEIGHT POUNDS
1 MONTH AFTER THERAPY DISCONTINUED
3 MONTHS AFTER THERAPY DISCONTINUED
4 MONTHS AFTER THERAPY DISCONTINUED
6 MONTHS AFTER THERAPY DISCONTINUED
1 YEAR AFTER THERAPY DISCONTINUED
2 YEARS AFTER THERAPY DISCONTINUED
DAYS

Figure 1.

they received no therapy other than folic acid.

The following case history of a patient with nutritional macrocytic anemia shows the hematologic and clinical response to folic acid therapy and the failure to develop subacute combined degeneration of the spinal cord.

Case 1—C. W., a 75-year-old white man, was admitted to the Hillman Hospital in December 1945 complaining of diarrhea, soreness of the tongue, and weakness. The family history was irrelevant.

He considered his health excellent until seven years prior to his admission when he began having infrequent bouts of diarrhea associated with cramping pains in the abdomen, anorexia, soreness of the tongue, and weakness, which usually lasted from two to three weeks and occurred chiefly during the spring and summer months. On two occasions during the preceding seven years, treatment with nicotinic acid had relieved the characteristic pellagrous glossitis, the epigastric distress, and the diarrhea.

A DIETARY history revealed that as long as the patient could remember he rarely had eaten meat, eggs, milk, or fresh fruit. His diet had consisted chiefly of liberal amounts of cornbread, grits, salt pork, dried vegetables, and occasionally green vegetables. Six weeks before his admission, he began having a moderately severe watery diarrhea, cramping pains in the abdomen, and anorexia. His tongue felt thick and sore at the tip. He developed occasional cramping pains in his legs, dyspnea and cardiac palpitation on exertion. General weakness progressed and during the six-week period following the onset of his illness, he lost 13 pounds in weight.

Physical examination showed an extremely pale, well-developed man who appeared chron-

ically ill, very weak, and considerably underweight. The tongue was thick, the papillae hypertrophied, and it was abnormally red, especially at the tip. Examination of the heart, lungs, and neuromuscular system disclosed nothing remarkable.

Laboratory findings—Gastrointestinal series was negative; a barium enema showed "the sigmoid and descending portions of the colon dilated and the entire colon spastic—no filling defects." Urinalysis, Kahn blood test, and spinal fluid were negative. Gastric analysis, using Ewald's meal, showed no free hydrochloric acid in the fasting specimen, 21° and 30° of free hydrochloric acid in fifteen and twenty minutes respectively, following the test meal. The initial blood findings were: red blood cells 2,350,000, hemoglobin 9.0 gm. (50 per cent), reticulocytes 0.6 per cent. Examination of sternal bone marrow showed typical arrest at the megaloblastic level. All the observers concurred in the diagnosis of nutritional macrocytic anemia.

After baseline determinations were completed, the patient was given 10 mg. of folic acid daily by mouth. On the eighth day of therapy, the reticulocytes reached a peak of 21 per cent. By the end of the fourth week on therapy, the red blood cells numbered 3,910,000, hemoglobin 12.8 gm. (83 per cent), and reticulocytes 1.8 per cent.

On the third day of therapy, the patient volunteered that he was hungry for the first time in many months and he ate all the food offered on the experimental diet. The following day he asked for additional servings of food. By this time, his tongue was no longer sore and the epigastric distress had disappeared. The diarrhea gradually subsided and had disappeared by the end of a week on therapy. His strength returned and by the time he was discharged four weeks after the initiation of therapy, he had gained 15 pounds in weight. At this time, his red blood cell count was 3,910,000, hemoglobin 12.0 gm., and reticulocytes 1.8 per cent. In the two and one-half years which have elapsed since he was discharged, he has had no recurrence of anemia or other symptoms, and frequent neurologic examinations have revealed no evidence of nerve involvement.

The following case history of a patient with Addisonian pernicious anemia illustrates the hematologic and clinical response to folic acid therapy, the subsequent development of subacute combined degeneration, and its relief following liver extract therapy.

Case 2—T. R., a 68-year-old white male cabinet maker, was first treated for pernicious anemia in 1931 by means of liver extract. At that time he was sick, had soreness of the mouth and tongue, and anorexia and dyspnea on exertion. He recovered rapidly and soon returned to work.

He occasionally ate liver and took liver extract at irregular intervals and in varying amounts with the result that he had a relapse during the summer of 1945. He took 10 mg. of folic acid daily by mouth. The initial counts were: red blood cells 1,980,000, hemoglobin 8.4 gm. (55 per cent), reticulocytes 1.0 per cent, white blood cells 3,500, and packed-cell volume 37 per cent. His blood responded well.

Symptoms related to the neuromuscular system first developed in the summer of 1946 with insidious onset of numbness of the feet, which gradually spread to the knees, and slowly increasing difficulty in walking; knee and ankle joints would give way, he would stub his toes, sway and fall. However, he stated that he worked efficiently making cabinets until about three and one-half weeks before his admission to the hospital; at that time he became disabled "overnight." There was a rapid increase in the severity of the paresthesia of the lower extremities, numbness and tingling and fleeting superficial pains of feet, legs, and lower half of the thighs; his hands felt numb and tingled for the first time; he could not walk without holding to the furniture in his room, could not step without watching where he placed his feet, and the lower extremities were hardly strong enough to support his weight.

On admission to the hospital in August 1947,

he appeared well-nourished and in no apparent distress while at rest in bed. There was very slight pallor of finger tips and conjunctivae; no icterus was noted; scalp hair was gray. The pupils were slightly irregular and reacted sluggishly to light and accommodation; hearing was moderately impaired for conversational tones; his tongue was almost smooth and the tip and margins were light red; the buccal mucosa generally was slightly hyperemic and a superficial fissure extended laterally from the right corner of his mouth externally. Heart and lungs were normal; there was slight tenderness in the lower abdomen. Anal sphincter tone was normal. The bicep reflexes were slightly hyperactive and knee jerks and ankle jerks equally hypoactive; the plantar reaction was plantar flexion; abdominal reflexes were absent.

There was no vibratory perception at the ankles and knees, very slight at the pelvis, but good at the wrists. There was slight to moderate impairment of pain and light touch sensation of feet, legs, and lower thighs, and of hands and fingers to near the wrists. Position-motion sensibility of the toes and ankles was markedly impaired. There was marked ataxia of lower extremities and very slight of the uppers; he was unable to arise to standing position alone, and could not walk without great assistance; there was slight tenderness over lower legs. The sensorium apparently was clear but he was quite easily disturbed emotionally.

A GASTRIC analysis showed no free hydrochloric acid after histamine and tests for the presence of rennin and pepsinogen were negative. The urinalysis, stool examination, and Wassermann blood test were negative; gastrointestinal x-ray study was negative.

He was given 2 cc. of refined liver extract (Reticulogen) daily for thirteen days, then 1 cc. daily thereafter for seven days. The dose was then decreased to 1 cc. per week. The patient improved rapidly on Reticulogen therapy. Despite the fact that he had some residual neurologic symptoms and physical signs, he returned to his job as a cabinet maker eighty days after treatment was started and has continued to work each day without interruption.

In another series of three cases of Addisonian pernicious anemia, one with severe and two with mild subacute combined degeneration, we have seen remarkable improvement following the parenteral injection of vitamin B_{12}. Prior to the injection of the bright red crystals of vitamin B_{12}, each of the patients complained of pain, tingling, and stiffness in the extremities. Following the administration of 15 micrograms of this material intramuscularly to each patient, Case 1, which was acute, remarked that the numbness, tingling, and pain diminished progressively during the first ten days after the injection. Stiffness and feeling of enlargement of the joints likewise subsided and allowed the patient to walk with ease. Within two weeks, there was remarkable improvement in the clinical findings of peripheral nerve-posterior column involvement.

Case 2, which was severe, noted decreasing amounts of pain, tingling, and coldness of the extremities. Three days following the injection, her feet perspired for the first time in months. During the two weeks' time, there was slight improvement in the physical findings, though this was less definite than in the first case.

Case 3, who had chronic peripheral nerve-posterior column involvement, observed diminishing paresthesia and stiffness of the extremities which improved locomotion considerably. During the two-week interval, there were no significant objective physical changes except apparent improvement in locomotion.

The fact that three patients with achlorhydria, Addisonian pernicious anemia, and combined system disease all volunteered relief of symptoms following parenteral injection of 15 micrograms of vitamin B_{12} is of very great interest in this regard.

SUMMARY AND CONCLUSIONS

1. A two-year study of the effect of synthetic folic acid in persons with macrocytic anemia in Birmingham, Alabama, and Havana, Cuba,

confirms and extends previous observations that folic acid is an effective anti-anemia substance capable of producing a clinical response and hematologic remission in persons with nutritional macrocytic anemia, tropical sprue, and the macrocytic anemia of pellagra and pregnancy.

2. It has long been known that subacute combined degeneration develops in persons with Addisonian pernicious anemia. This study shows that folic acid stimulates the bone marrow in this disease without preventing the neural disturbances. Twenty-eight of the 38 cases in this study who were observed over a period of two years developed subacute combined degeneration. Irrespective of how much folic acid was administered to these persons, it became worse until liver extract was administered. Following massive liver extract therapy, it was promptly relieved. In every instance in which subacute combined degeneration developed in this series, the patient had gastric achlorhydria on repeated tests following histamine stimulation, prior to folic acid therapy.

3. In contrast to the persons with Addisonian pernicious anemia, those with nutritional macrocytic anemia, tropical sprue, and the macrocytic anemia of pregnancy in this series did not have histamine refractory achlorhydria either previous to or during therapy with folic acid and in no instance did any evidence of subacute combined degeneration develop. These findings suggest an important relationship between histamine refractory achlorhydria and the development of subacute combined degeneration.

4. These findings suggest that folic acid therapy is analogous to therapy with niacin, thiamine, and other vitamins of the B complex and that its administration is effective for certain manifestations. In the eighteen years in which the senior author has been working with clinical deficiency diseases, he has seen much evidence to support the concept that vitamin deficiency diseases in human beings tend to be multiple in nature. The administration of a specific vitamin corrects for a deficiency of itself and often aids in improving the general health and well-being of the patient but it cannot correct a deficiency of all of the essential dietary nutrients. Patients who remain on an inadequate diet and return to work tend to relapse sooner than those who remain at rest.

5. In another series of three patients with achlorhydria, Addisonian pernicious anemia, and subacute combined degeneration of the spinal cord, all volunteered relief of symptoms following the parenteral injection of 15 micrograms of vitamin B_{12}. The subjective improvement in all three patients was remarkable; and in the case which was most acute, there was considerable improvement in physical signs.

REFERENCES

1. Fenwick, S.: Lancet 2:78 (July 16) 1870.
2. Castle, W. B., Heath, C. W., and Strauss, M. B.: Observations on the etiologic relationship of achylia gastrica to pernicious anemia IV. Am. J. M. Sc. 182:741, 1931.
3. Leichtenstern, O.: Deutsche med. Wchnschr. 1884, p. 849.
4. Nonne, M.: Arch. f. Psychiat. 25:421, 1893.
5. Rundles, R. W.: Prognosis in the neurologic manifestations of pernicious anemia. Blood 1:209-219 (May) 1946.
6. Spies, Tom D.: Experiences with folic acid. Chicago, The Year Book Publishers, 1947, 110 pp.
7. Spies, Tom D., and Stone, Robert E.: Some recent experiences with vitamins and vitamin deficiencies. South. M. J. 40:46-55 (January) 1947.
8. Spies, Tom D., and Stone, Robert E.: Liver extract, folic acid, and thymine in pernicious anemia and subacute combined degeneration. Lancet 1:174-176 (February 1) 1947.
9. Vilter, Carl F., Vilter, Richard W., and Spies, Tom D.: The treatment of pernicious and related anemias with synthetic folic acid; observations on maintenance of normal hematologic status and on occurrence of combined system disease at end of one year. J. Lab. & Clin. Med. 32:262-273 (March) 1947.
10. Heinle, Robert W., and Welch, Arnold D.: Folic acid in pernicious anemia; failure to prevent neurologic relapse. J.A.M.A. 133:739-741 (March 15) 1947.
11. Ross, J. F., Belding, H., and Paegel, B. L.: The development and progression of subacute combined degeneration of the spinal cord with pernicious anemia treated with synthetic pteroylglutamic (folic) acid. Blood 3:68, 1948.

Small, Commonly Unrecognized Strokes

WALTER C. ALVAREZ*

MAYO CLINIC, ROCHESTER, MINNESOTA

One of the commonest diseases of man is the slow petering-out toward the end of life, and one of the commonest reasons for such petering-out is the gradual destruction of parts of the brain by repeated thromboses of small sclerotic blood vessels. As Osler said, many persons take as long to die as they did to grow up, and they live a sort of death in life. Recently I heard of a patient who was thirty years a-dying. The process began with three apparently small strokes at the age of 57. They did not affect muscles or skin or speech, but they so crippled the man mentally that he had to retire from business. Following this, he was somewhat childish, very forgetful, and a terrible problem in his home. He lived on in this state, and died at the age of 87.

SMALL INFARCTS OF THE BRAIN ARE COMMON

As neuropathologists have pointed out, at necropsies of older persons with arteriosclerosis, one commonly finds any number of tiny infarcts in the brain. The problem is to correlate these infarcts with episodes during life.

*Division of Medicine, Mayo Clinic, Rochester, Minnesota.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

One would think that there must have been little spells of some kind, perhaps with giddiness or headache or a faint, but often the patients' physicians made no note of any such episodes. In many cases they diagnosed only acute indigestion, or a little Meniere's disease, or an upset liver.

SMALL STROKES COMMONLY GO UNRECOGNIZED

Every so often I see an older person with troubles which I think represent the residue of a little stroke partly because they came suddenly at a certain moment of a certain day. In most of these cases the history, as taken by an intern or assistant, is not good enough to reveal what actually happened; the physician must think of what might have happened and then must draw forth the typical story. Too often he does not think of a stroke, or if he does, he may dismiss the idea as preposterous. However, if he were to take an adequate history he would see that with the short fainting spell, or the spell of dizziness, or distress in the thorax or abdomen, there came a marked change in temperament and memory and ability. Perhaps after the little episode the patient was never again able to do a bit of work or to enjoy one moment of life. To me these facts are always highly significant.

THE PATIENT OFTEN GUESSES WHAT HAPPENED

OFTEN the patient realizes what happened to him even when his doctors do not. Many times I have said to a patient, "Haven't you a pretty good hunch as to what happened to you?" And the man answers, "Yes, at the time I was almost certain I was having a stroke, and that is what I now think I had." As a sweet little old lady once said, with great clearness of vision, "Death has been taking little bites of me!" She saw that with each dizzy spell, or fainting spell, or spell of confusion, or severe headache she became a little older, a little weaker, a bit more tired, her step more hesitant, her memory less trustworthy, her handwriting less legible, and her interest in life less keen. She realized that for some ten years or more she had been moving step by step toward the grave. Her doctor hooted at the idea, but *she* knew what was going on; she knew that something seriously wrong was taking place in her brain.

WALTER C. ALVAREZ

THE DISEASE AS A WHOLE HAS NOT BEEN DESCRIBED

Curiously, this common disease is almost unknown today; cases of it are never shown to medical students; articles on it are practically never read before medical societies, and when I searched through the books, journals, and the larger systems of medicine, hunting for an adequate description of this disease, I could not find one. I found, of course, descriptions of some syndromes due to cerebral arteriosclerosis, and to spasms of intracranial blood vessels, but nowhere did I find a picture of the disease as a whole—the disease which begins commonly in the forties and gradually pulls the patient down into his grave.[1]

THE NEED FOR QUESTIONING RELATIVES AND FRIENDS

Often I see cases in which a man's wife and family and business associates realize that something terrible has happened to his brain; they know that he is not the fine, sensible, kindly person that he was before he had his big dizzy spell, and they know that he can no longer carry on in his business. He has lost his drive and his judgment and his ability to get things done. Often the family physician who has known the man for years knows that he is greatly changed, and oftentimes he realizes that there must have been a stroke. It is the city consultant who commonly misses the diagnosis because he fails to draw forth the story, and depends on tests which show nothing. Furthermore, he depends on the history the patient gives him and he does not question the wife and relatives and friends who are far more likely to give him the essential information as to deterioration of character.

PHYSICIANS ARE RELUCTANT TO DIAGNOSE A STROKE

Curiously, most of us physicians hate even to mention strokes, and we hate to face the situation; we dodge it and make some other

diagnosis. Usually, we refuse to talk honestly to the patient about his real trouble. I wonder if we are still influenced by the old idea that there is something disgraceful about a stroke—that it came because God was angry with the man and struck him down. Many persons believe that. Obviously, we physicians know better; we know that all that happened was that a little artery which had become narrowed because of disease suddenly plugged up.

One difficulty I have had in convincing some doctors that their patient had a little stroke was my inability to convince them that the brain had been injured. They said, "But the man has no neurologic signs." My answer was that to my way of thinking a decided change in character, or a great loss of memory, or a sudden nervous breakdown, or a marked loss of interest in grooming, or a change in handwriting, or a thickening of speech, is a neurologic sign.

Another thing we physicians often do, when perhaps we admit that something went wrong in the brain, is to maintain that there was only a temporary spasm of a vessel. Although it is probable that in some cases this is true, in most cases it is not. Pathologists believe now that in most cases there was a thrombosis.

Another trouble with us physicians is that commonly we forget that the brain is an organ of the body and that it should have a lot of diseases all its own. Our peculiar training in medical school has left us without any tendency to think of the brain. If a man drops down in a faint and dies a few days later, we say he had a heart attack. He may have had, but he may also have had a vascular accident in his brain.

Perhaps the main reason why this very common disease of slow dying is not well known to the medical profession is that different physicians generally see the patient in his different episodes, and hence they do not get any idea of the disease as a whole. This can be gotten only by a physician who practices among families, or best yet, by one who has a chance to watch the slow unrolling of the disease in some of his older relatives.

A TYPICAL CASE OF SLOW DETERIORATION

The first patient who started my study of this disease and the one who eventually caused me to recognize it in its entirety was a relative of mine, an able college president who, during the middle half of his life, had several curious nervous breakdowns. The first came at about the age of 33 years and the next about six years later. On each of these occasions he had to take a year off to recuperate. As I did not know him then, I cannot give details about his illness, but some of the able physicians who saw him then thought that the trouble was with his kidneys. A few thought he might have a smoldering tuberculosis. Subsequent events indicated that they were wrong, and what the man probably had were episodes in the course of the long disease which eventually killed him.

After he had recovered from his second sudden illness and nervous breakdown, he had to take an easier job. About two years later he had a sudden severe shock and almost died. It was thought to be a heart attack, but this is very unlikely because during the years that followed the man never showed any symptoms or signs of heart disease. Evidently he had had a good-sized stroke, because signs of deterioration in character promptly appeared. Formerly a lovable Irishman, he now became irritable and irascible. Formerly he was most careful about the cleanliness of his body and his clothes; now his wife had to insist that he bathe and change his linen. Formerly well mannered at table, he now ate coarsely. His business associates noticed the marked change in grooming and the changes in his character, and thought that he must be tippling in secret or taking some drug.

Later, he apparently had a little stroke which hit his bulb and left his swallowing mechanism so impaired that at mealtimes a little food would enter his larynx and cause much coughing. This difficulty continued until the end of

his life. By this time he was a terrible problem at home because of his unreasonableness.

A little later a wealthy friend gave him a trip to the Orient, thinking that the vacation would do him good. There he had another sudden illness, after which he didn't write to his wife for nearly two months. His physician should have noted the significance of this, because previously, when on trips, he had always written a daily letter. On his return from the trip he forgot even to express thanks to the friend who had given him the vacation. This showed a big change in character, because previously he had been so polite and gracious and so punctilious about giving thanks.

After this, the man became so careless about his clothes and appearance that he had to resign from his company. He dribbled urine so that he came to reek of ammonia. Curiously, he didn't seem to notice the odor or to feel any embarrassment about it when in company. Then, one morning, on getting out of bed, he found one leg too weak to hold him up. This passed off in an hour or two but, at last, and for the first time in his illness, the true nature of one of his episodes was suspected by his physicians. Here was something that they could give a name to. During the few years that followed, he had many more little spells and finally he died, at the age of 57, of a big stroke. He died a purely brain death, his heart and kidneys and other organs working well right up to the end.

It was only after I had watched the progress of this man's illness for years that I came to realize that the episodes were all part of one disease. Later, I watched episodes such as he had had pull down others of my relatives and friends.

ANOTHER CASE

The wife of the man whose condition I have just described began to have recognizable little strokes at the age of 57. For the first time in her life she became ill. She would get a little dizzy spell, and would then feel tired and weak. She had to cut down markedly on her activities. For years she had had a systolic blood pressure of around 200 mm. of mercury. At the age of 59 she had a big stroke, with hemiplegia and complete aphasia. With this her weight dropped from about 190 to 100 pounds (86 to 45 kg.). Destructive changes promptly appeared in the right hip joint on the same side as that of the paralysis. Her blood pressure dropped to normal, and remained that way for the rest of her life. With this stroke she lost all her old feeling of good health; she became utterly miserable; she said she felt awful, and had lost all joy in life. Fortunately, she kept her sweet character, and many of her interests in business and family.

During the remaining six years of her life I watched her have attack after attack of dizziness, nausea and vomiting, and sometimes much mental distress; sometimes she would be prostrated in bed for a few days after one of these jolts. When she died, necropsy showed her brain to be speckled with scores of little brown infarcts. There were enough, and more, to account for all the dozens of little episodes that she had had. There was no need to invoke the idea of temporary *spasms* in blood vessels. There was no other lesion in her body to account for the long illness and death.

Naturally, these little strokes are most likely to appear in the sixties or fifties or forties, but they can be found in the thirties, and during the second World War they were observed even in soldiers in their late twenties.

PARESTHESIAS REFERRED OUT FROM THE BRAIN TO THE THORAX OR ABDOMEN

I, who am supposed to be a gastroenterologist, often see these people because a little stroke was accompanied by some sort of storm down the vagus nerves, or by a curious distress, or pain referred out into the abdomen. For instance, a physician one day suddenly felt as if something were torn in two in the abdomen. Careful studies at a hospital failed to show anything wrong, and there was no sign of shock such as there would have been if something had gone wrong in the abdomen. Later, there

was a similar episode with a similar prostration. On both occasions the patient had to stay in bed for some time because of great weakness and apathy. In many of these cases the wave of heat or distress or pain is referred into the thorax and is then mistaken for a symptom of angina pectoris.

MANY STROKES CANNOT BE RECOGNIZED AT THE TIME

Sometimes I am fairly certain that a patient's illness is due to one or more little strokes, but I cannot get a history of them. Sometimes I think I might if I could interview members of the family or the business entourage. One difficulty is that many small thromboses probably come during the night when the blood pressure is low. Then the patient may wake with "a head on him" or much of his memory gone. Other strokes, which come in the daytime, are not associated with feelings of shock and therefore are not recognized for what they are. It is interesting to note how bad a stroke a man can have without feeling any shock or pain. I have seen men fall to the floor with a bad hemiplegia, but without any feeling of shock or mental distress.

Most small strokes do not produce any of the ordinary neurologic signs of nerve or brain injury, because there are so many places in the brain in which one can put a good-sized area of destruction without producing any weakness of a muscle or any patch of anesthesia in the skin.

Often I have been uncertain about the nature of a suspected episode until the patient came back two or three times with the story of some much more definite, little or big strokes. Sometimes a patient will say that he fell or slipped or stumbled or miscalculated the height of a step, but the fact that for weeks or months afterward he was a bit confused or dizzy or unable to work, makes it seem more probable that his fall was due to a slight stroke. Many attacks of so-called acute indigestion are really little strokes.

DETAILS WHICH SUGGEST THAT THERE MAY HAVE BEEN A STROKE

With many a small stroke the blood pressure suddenly falls to normal. Such a fall, I think, is fairly pathognomonic of a little stroke. Sometimes the pressure goes back up, but sometimes it does not.

A sudden, inexplicable loss of weight may also be due to a little stroke. In the case of the woman whose story I have given in this paper, there was, after her big stroke, a prompt loss of about 90 pounds (41 kg.). I have commonly seen losses of 40 or 50 pounds (18 to 23 kg.).

I have already mentioned the distressing pains, paresthesias, or "heat-waves," or rending feelings that are referred out from the brain to the thorax or abdomen. Sometimes, after such a wave, there will be a spasm of the stomach so that food entering it will be rejected or will cause cramping. This spastic state may pass off in a couple of months.

Symptoms of slight bulbar paralysis must be watched for, and their significance recognized. Often a little stroke which hits the bulb will interfere with swallowing; it may produce ropy saliva, or thickness in the speech.

Occasionally there will be a slight patch of anesthesia somewhere, or a little weakness of some muscle or some uncertainty in using hands or feet. Many persons say they feel top-heavy, or uncertain, or giddy. They feel that if they were to turn a corner quickly while looking up, they might fall down.

Most convincing often to me is a sudden change for the worse in the personality. For instance, a man who all his life had been a tower of strength to his family, always kindly, thoughtful, and considerate, and never for a moment complaining or thinking of himself, suddenly became a querulous invalid who could talk of nothing but his discomforts and his bowels that wouldn't move as they used to. No longer could his relatives come to him with their troubles; he had too many of his own. Later, there came a mild parkinsonian syndrome. Incidentally, such a syndrome late in life is probably often due to little strokes.

Sometimes, especially if a patient has much insanity in his family, with a little stroke there will come psychopathic changes. An older person will become suspicious of formerly adored children, or he will become penurious, or he may even do some things which are immoral. He may lose his business judgment and may dissipate his fortune. Often, after a man has fallen out of his chair or has fallen down in his office, he will no longer initiate anything, and his department will run down and the younger men in it will leave. In many cases such a patient becomes a terrible problem in the home, where his care is exceedingly difficult. He may fight with his children and his grandchildren. A woman, formerly a devoted wife and mother and grandmother, will no longer take any interest in home, husband, children, grandchildren, or friends. She may refuse to see old friends.

Occasionally, after a little stroke, a man or woman will go into an agitated depression. I remember several such women who walked the floor, wringing their hands and crying, and saying that their suffering was more than they could bear.

Rarely, there will be a sudden coming of insomnia in a person who always slept well before. More frequent is the coming of a fear of being left alone. Probably the man who has had a little stroke becomes much afraid of another, and hence will not stay alone if he can possibly help it.

Another symptom which I think is sometimes due to a little stroke is a burning or a bad taste in the mouth without any local lesions. This symptom is commonly seen in the cases of women around the age of 50.

Atypical facial pains in older arteriosclerotics may well be due to a little stroke. I remember a wealthy physician with such pain, who on several occasions had all his ganglions and much of his face on the affected side anesthetized with procaine, without experiencing the slightest diminution in the severity of his distress. This suggested that the lesion was higher up, in his brain; the man had had some little strokes before his pain came, and he eventually died with a series of them.

Sudden blindness occurs in some of these people, usually in one eye.

Arthritis with trophic changes may also come on suddenly in one extremity.

The attacks which probably are due to *spasm* in a small vessel are rather characteristic. A man may have an aphasia lasting for half an hour and then he will get perfectly well; he may have another one the next day and the day after that, and then he may go for a year without any more.

In diagnosing these little strokes I think the essential point often is the history of a sudden onset. Highly important also is a history of a change of character.

PROGNOSIS

THE prognosis is usually not very good if there is marked change in character. These are the tragic cases. In other cases after two or three small strokes I have seen a man or woman have to wait for fifteen or twenty years before there came another jolt.

TREATMENT

Obviously, in many cases there isn't very much that can be done in the way of treatment. Probably the best thing to do is not to allow anyone to treat the patient too much. One shouldn't deprive the person of all the pleasures of living such as eating, smoking, drinking, and walking about and visiting friends. No effort should be made to reduce the blood pressure. Theoretically, it is best for the circulation of the brain if the blood pressure remains high.

Should the person be told what is wrong? I think that usually, if one is dealing with an intelligent person, it is best to talk frankly. Often the patient knows what happened, and then he or she is bound to feel much better if the doctor talks honestly about the diagnosis and the chances of recovery or continued living.

REFERENCE

1. ALVAREZ, W. C.: Cerebral arteriosclerosis with small, commonly unrecognized apoplexies. Geriatrics 1:189-216 (May-June) 1946.

The Climacteric in Women and Men

AUGUST A. WERNER*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

THE TERM menopause, literally meaning cessation of menstrual flow, is commonly used to designate that critical period in a woman's life, more correctly spoken of as the climacteric. Menstrual pause may occur at any time during active sexual life from various causes. Disturbances of menstrual flow, such as irregularity, profuseness, scantiness, or cessation are only visible evidences that there is some disturbance of the function of the glands which control the menstrual mechanism.

Some women believe that when menstruation ceases at the climacteric, that they are through the change of life. They are mistaken, for menstruation ceases only because the ovaries do not function sufficiently to produce the endometrial changes that result in bleeding. It is the decrease or absence of ovarian function that initiates all of the difficulty, and not the absence of menstruation. The disturbance of, or the cessation of menstruation is only one of the phenomena which occur at the climacteric. It is the one sign which is objective and therefore it attracts most attention, but it is far from being the most disturbing factor of the climacteric.

Menopause marks the end of the child-bearing period in a woman's life. The ovaries, which have been primarily responsible for the sex life of the individual, begin to lose their function and their responsiveness to stimulation by the pituitary gland, which is their activator. The pituitary gland becomes secondarily disturbed, and since the pituitary exercises stimulatory influence on other glands, such as the thyroid and the adrenals, a complex crisis, or climax, occurs.

The climacteric is further complicated by the fact that these ductless glands exercise varying degrees of influence on the two nervous systems, namely, the central or voluntary nervous system and the autonomic or involuntary nervous system. Both nervous systems are interrelated, but the autonomic nervous system is seemingly more disturbed, for it is the nervous network which controls the vital life processes of the organism, over which we have no control at all.

Among physiologic activities which are under autonomic control may be mentioned the emotions to a great extent, the sense of physical and mental well-being, the heart and the respiratory rates, the digestion of various foods,

*Assistant Professor of Internal Medicine, St. Louis University School of Medicine.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

and the marvelous chemical reactions which occur in the body and the various tissues, especially in the liver.

With disturbance of function of the ovaries and other interrelated glands and the imbalance of the nervous systems, a train of subjective symptoms occurs, which renders the patient uncomfortable and in many instances are very distressing. Perhaps most women experience some discomfort at the climacteric, but in many it is so mild as to be negligible. Others have a more severe disturbance and in these women the symptoms can be alleviated by proper treatment with estrogens.

It is important that the duration of the climacteric be stressed. The climacteric varies in duration with each individual. Some women enter the climacteric at about 38 years of age, while others do not experience difficulty until they are approximately 50 years of age; the average age is about 40.8 years.[1, 2] It must be remembered that a woman need not be of climacteric age to have all of the symptoms characteristic for the menopause. Since these symptoms are initiated by ovarian hypofunction or afunction, they will occur in castrates and younger women who have decreased function of the ovaries, regardless of age. A woman will not be free of symptoms until she develops the glandular equilibrium characteristic for the postmenopausal period.

In some women endocrine balance may occur within three to six months, while in others the imbalance may last five, six, or even more years. There are also some women who claim not to have had any appreciable disturbances at the time of cessation of menstruation, and who perhaps five to ten years later, at ages of 50 to 60 years, develop the typical symptoms of the climacteric; there may be a renewed, but unsuccessful attempt by the pituitary to stimulate gonadal function. This has been described by the author as the postmenopausal syndrome. Practically all of these women respond favorably to treatment with estrogenic hormones.

Hypoovarianism may be caused by disease conditions such as the degenerative or inflammatory processes in, or adjacent to the ovaries, as inflamed tubes or appendicitis, which may cause degeneration in the glands. It may be secondary to constitutional disease processes as in certain anemias, tuberculosis, or malignancies. Vitamin deficiency in the diet may be a cause. It may be primary as in some cases in which the ovaries fail to develop or attain complete function. It may be secondary to secretory deficiency of the pituitary, as in some types of infantilism or obesity. It may occur after partial castration when one ovary has been removed or only a small part of one ovary remains. It will be complete when both ovaries are removed, unless there is accessory ovarian tissue. It always occurs at some time during the climacteric.

SYMPTOMS CHARACTERISTIC FOR OVARIAN HYPOFUNCTION, AFUNCTION, AND THE CLIMACTERIC

Disturbances which accompany ovarian hypofunction and afunction and which occur, especially at the climacteric, may be divided into objective signs and subjective symptoms.[1-11]

Objective signs—The objective signs include various types of menstrual disorders occurring separately or with varying degrees of combination, such as irregularity, scantiness of flow with decreased duration (hypomenorrhea), and finally, cessation of menstruation (amenorrhea). Excessive bleeding at menstruation (menorrhagia) and profuse irregular bleeding between the menstrual periods (metrorrhagia) are more apt to occur in women who are approaching the natural menopause than in those of younger age. In castrates, the cessation of bleeding follows the operation, if all ovarian tissue has been removed.

Obesity, second objective sign, is characterized by a generalized deposition of fat, or a localized deposition over the trochanters and fatty enlargement of the breasts. The localization of fat over the trochanters and in the breasts usually occurs in younger women who have ovarian hypofunction and in castrates after they reach the age of approximately 30

AUGUST A. WERNER

years. Many obese girls, when they attain the age of puberty, have delayed, irregular, or scanty menstruation, or they may have complete absence of menstruation; this is usually due to a complex endocrine disorder.

Following the termination of pregnancy, a complicated endocrine readjustment must occur in the woman, and frequently the glands do not strike a normal balance, with the result that many women have various types of menstrual disorders and some of them date their onset of obesity from one of their pregnancies. Other signs of ovarian hypofunction or afunction are atrophy of the genitals and breasts and loss of genital and axillary hair.

Subjective symptoms—The subjective symptoms accompanying ovarian hypofunction or afunction render the patient more uncomfortable than do the objective signs. These subjective symptoms may be classified as nervous, circulatory, and general in origin. A proper evaluation of their significance is necessary as these symptoms are the chief basis of diagnosis of ovarian hypofunction or afunction.

Subjective nervousness is an intense feeling of nervous tension. Many patients state that they feel jumpy, or trembly inside their body; a common expression is that they have "butterflies in the stomach." Some state that they feel like screaming, or as though they might lose their mind. In most instances, they do not have a tremor, but occasionally this nervousness may become so extreme as to cause some tremulousness. (Table 1.)

Excitability is a nervous state in which the persons respond to ordinary stimuli in an exaggerated manner, especially in regard to their psychic reaction. Unfavorable news, slight mishaps, arguments, all manner of little occurrences that would not disturb a normal individual cause quite a nervous and mental flurry.

These people are very irritable and easily aggravated or excited to anger by deed or word. They are hard to please. Noises of playing children, the radio, almost anything stirs them to action. In fact, they need no special stimuli; they are simply hard to get along with. In many instances they acknowledge this condition, but state that they cannot help being so.

HEADACHES of various types and locations occur, but they are rarely migrainous. Migraine is a sick headache, usually unilateral, and may be accompanied by nausea and vomiting. When migraine occurs with endocrine disorders, it is probably only initiated or aggravated by the glandular irregularity.

The usual headaches may be described by the patient as dull to severe aches, not neuralgic in type. They may occur irregularly, or be continuous. Patients have been observed with headaches lasting continuously for thirty to forty days which were relieved by proper endocrine treatment. Their location may be temporal, frontal, or supraorbital, and there may be a sensation of retro-orbital pressure which may cause the eyes to ache.

There are two types of headaches which have almost specific diagnostic importance in hypoovarianism, vertex and occipitocervical.

TABLE 1
FREQUENCY OF NERVOUS SYMPTOMS IN WOMEN

	53 Castrates Per Cent	96 Menopause Per Cent	48 Involutional Melancholia Per Cent
Nervousness, subjective	100.0	92.7	100.0
Excitability	84.2	72.9	100.0
Irritability	68.0	61.4	95.8
Headache	36.0	50.0	83.3
Occipitocervical pain	58.0	37.5	56.2
Decreased memory and concentration	51.0	54.1	95.8
Depression, crying	71.7	60.4	100.0
Psychosis	20.8	35.4	100.0
Formication	23.1	23.9	29.2
Sleep disturbed	66.0	59.3	72.9

Patients describe the vertex ache as if a great weight were resting on the head and some state that they feel as if the top of the head wanted to push out.

Occipitocervical aching is located in the occiput and it radiates to the nape of the neck and at times over the shoulders or down the spine. It is described as a severe, dull combination of ache and pain which may be continuous for days. When this ache is present many patients say their minds are hazy or fogged.

Among nervous symptoms may be classed psychic depression, commonly called "the blues." When in this state these patients have no special interest in ordinary activities. They cannot "cheer up." It is an effort to smile or laugh, they do not want company or care to enter into pleasurable entertainment. Frequently this depression is accompanied by crying for no reason at all. They state that they cannot prevent this. This condition, if untreated or unimproved, may progress to anxiety psychosis in which the patients feel ill at ease. They have a fear of impending danger which they cannot explain. They worry unnecessarily and feel that something dreadful will happen to them, their loved ones or others. Some patients whose past life had been rather Bohemian develop an extremely religious outlook.

Decreased memory and ability for mental concentration are observed. Patients forget where they put things. They cannot remember, especially recent events. The mental processes are slow and they cerebrate slowly. The mind seems hazy or fogged. If they read an article they cannot tell what they have read and frequently must reread it three or four times before it registers.

Formication, a sensation as if ants or insects were crawling over the skin, especially on the arms, back, and body, is complained of frequently. There also may be prickling or tingling of the skin.

A LARGE majority of these patients complain of sleeping poorly. They may be restless, sleeping only for short intervals during the night. Some fall asleep quickly upon retiring only to awaken within a half hour and remain awake for varying lengths of time. Others do not sleep upon retiring until after midnight. Some complain that they sleep well until 2 or 3 A.M. and then remain awake until morning. Patients who do not sleep at night find themselves exhausted the next day and must sleep during the daytime. This desire to sleep during the daylight hours must not be confused with somnolence.

Hot flushes have always been considered positive proof that a woman was in the menopause. (Table 2.) This is not literally true, for some patients who have many climacteric symptoms do not have hot flushes. Hot flushes are characterized by sudden redness of the face and neck, upper chest and at times, most of the body, due to a dilatation of the superficial capillaries of the skin. It is a very uncomfort-

TABLE 2
FREQUENCY OF CIRCULATORY SYMPTOMS IN WOMEN

	53 Castrates Per Cent	96 Menopause Per Cent	48 Involutional Melancholia Per Cent
Hot flushes	94.3	91.6	81.2
Tachycardia, palpitation, dyspnea	54.7	72.9	79.0
Vertigo	68.0	71.8	62.5
Scotomata	43.4	50.0	12.5
Cold hands and feet	43.4	23.9	81.0
Numbness, tingling	37.7	29.1	77.1
Pulse average per minute	76.	78.3	76.
Blood pressure, average	123/76.	138/88.6	128/76.
Pulse pressure, average	47.	50.	52.

able sensation and generally is of short duration, but it may last for half an hour, or even longer if the statements of some patients are correct. Frequently the flushes are described as a smothering sensation. They may be accompanied by vertigo, scotomata, or tingling or prickling sensations over the head, neck, and body. They are frequently accompanied by profuse perspiration, and the patient may feel faint. Occasionally hot flushes alternate with, or follow chilly sensations over the same areas. Hot flushes may accompany disturbances of the heart and blood vessels, especially arteriosclerosis with hypertension, but these conditions can be eliminated by proper diagnosis.

These patients notice tachycardia, palpitation and dyspnea more than usual upon moderate effort, without any disease condition to account for it. They may awake at night with tachycardia and palpitation, which usually is of short duration.

They also complain of easy fatigability; sweeping, ascending a flight of stairs, walking a block to the store, almost any moderate effort causes them to fatigue more than normally and may be associated with mild to moderate palpitation, tachycardia, and dyspnea. Patients frequently state that they are more tired upon arising in the morning than when they retired.

Vertigo with change of position and even while changing position in bed, is another very frequent symptom. It is generally more annoying than serious. Tinnitus as a buzzing, hissing, or a ringing sound in the ears is frequently complained of.

FREQUENTLY there are scotomata as dark spots or silvery specks floating before the eyes. Vertigo, tinnitus, and scotomata often occur concurrently and of these vertigo is the most frequent. Cold hands, feet, and extremities are commonly found in this condition.

The pulse rate is usually not changed much unless there is thyroid disturbance. In some instances the blood pressure may be moderately increased but this usually returns to normal with proper treatment.

General symptoms—Constipation is very frequently found in people of climacteric age, but it is probably not a condition which is directly attributable to the endocrine disturbance. In the vast majority of patients, constipation is probably due to improper habits, diet, or gastrointestinal disorders. (Table 3.)

Patients complain of vague pains and their location may be as legion as is the distribution of the sensory nerves. One of the most common pains is a boring ache which may be located below the lower angle of the scapulae or in the center of the upper part of the back. Again, it may be anywhere along the spine, especially in the lumbosacral region and the legs may ache. Pain in the chest, over the region of the heart is frequently complained of; usually this pain over the heart is in the chest wall and is not caused by any heart condition.

There is a condition known as menopausal arthritis characterized by soreness in various joints throughout the body, without redness or swelling, which may last from a few days to

TABLE 3
FREQUENCY OF GENERAL SYMPTOMS AND SIGNS IN WOMEN

	53 Castrates Per Cent	96 Menopause Per Cent	48 Involutional Melancholia Per Cent
Lassitude, fatigability	75.0	78.1	98.0
Constipation	72.5	72.9	83.3
Vague pains	Not recorded	Not recorded	77.1
Obesity	28.0	51.1	8.33
	Chiefly gonad (43 cases recorded)	Pit. and thy. (86 cases recorded*)	Moderate obesity (4 cases recorded)
Menstrual disorder	100.0	97.7	100.0
Amenorrhea	94.3	41.5	37 more than 6 mos. 11 less than 6 mos.
Basal metabolism	+6.4 (6 cases)	+8.2 (17 cases) −7.0 (3 cases)	See special reference

*Obese before menopause, 18; after menopause, 26.

an indefinite period. The joints most commonly involved are those of the fingers, hands, wrists, shoulders, and the spine, especially in the lower part of the back. In some instances there is some thickening of the joints in the fingers, which are painful.

CLIMACTERIC PSYCHOSIS (INVOLUTIONAL MELANCHOLIA)

Probably the first biologic urges of primitive man were what are now called instincts. Closely associated with instincts are the emotions. The emotions represent psychic responses to internal and especially to external stimuli. These responses are mediated through the central and autonomic nervous systems and hormones of the endocrine glands.

It is known that hyperfunction and hypofunction of the endocrine glands can so disturb persons emotionally that they manifest psychoses. The hormonal conflicts of pregnancy and necessary readjustments following parturition may result in profound disturbances of the personality and psychosis.

After an extended observation of a large number of patients over a period of years, having mild to extreme menopausal symptoms, the author and associates concluded that so-called involutional melancholia is only the severest manifestation of the disturbances at this period in life. Knowing the efficacy of estrogens in relieving the distress of patients exhibiting the castrate-menopausal symptoms, we decided to treat a group of carefully controlled patients having involutional melan-

TABLE 4
SYNDROME ACCOMPANYING DEFICIENCY OR ABSENCE OF THE OVARIAN FOLLICULAR HORMONE IN 197 CASES (53 CASTRATES, 96 MENOPAUSE, 48 INVOLUTIONAL MELANCHOLIA)

	Order of Frequency of Symptoms	Per Cent
1.	Menstrual disturbances	99.2
2.	Nervousness, subjective	97.6
3.	Hot flushes	89.0
4.	Excitability	85.7
5.	Fatigability and lassitude	83.7
6.	Depression and crying	77.4
7.	Constipation	76.2
8.	Irritability	75.1
9.	Tachycardia, palpitation and dyspnea	68.8
10.	Vertigo	67.4
11.	Decreased memory and concentration	66.8
12.	Sleep disturbed	66.1
13.	Amenorrhea	57.6
14.	Headaches	56.4
15.	Psychosis	52.2
16.	Occipitocervical aching	50.6
17.	Scotomata	49.4
18.	Numbness and tingling	48.3
19.	Cold hands and feet	35.3
20.	Formication	25.4
21.	Vague pains (recorded for involutional melancholia)	77.1

cholia by administration of estrogen. This was done over a course of several years and the results obtained in this series of experiments were gratifying and have been published. Many other reports have since appeared in various medical journals by other physicians.

THE MALE CLIMACTERIC

Both men and women have a pituitary-gonad relationship and it is well established now that men are subject to decreased function of the sex glands, just as women are, especially in later life.

In the girl at puberty the gonadotrophic hormones of the pituitary stimulate the ovaries to function, with the development of a follicle in the ovary and the production of an ovum. The cells lining the follicle produce estrogenic hormone, which in turn stimulates development of the breasts, the internal and external genitals, and the configuration of the body, which changes from that of the girl, through adolescence, to womanhood.

In the boy at puberty the gonadotrophic hormones stimulate the testicles to function. The interstitial cells are stimulated and these secrete testosterone which initiates development of the secondary sex characteristics and the other changes, as he develops from boyhood, through adolescence, to normal manhood.

The most obvious and fundamental difference which occurs as a result of this pituitary-gonad relationship in the human male and female is that the normal woman menstruates.

The menstrual cycle may be looked upon as an extra phenomenon in the woman and not as an occurrence necessary for her sense of well-being. If the uterus is removed and the ovaries are healthy and their function is not disturbed, her pituitary-ovarian relationship will continue as it does in the man and she can and will feel perfectly normal, until the climacteric is reached.

TABLE 5

FREQUENCY OF CIRCULATORY SYMPTOMS IN THE MALE CLIMACTERIC

	Per Cent
Hot flushes	29.3
Chilly sensations	6.2
Sweating	17.9
Vertigo	46.5
Scotomas	26.0
Tinnitus	10.6
Numbness and tingling	43.9
Cold hands and feet	32.9
Tachycardia, palpitation and dyspnea	51.2

As a result of the over-emphasis which has been placed upon the cessation of menstruation in the woman and because the man does not have this phenomenon, it was believed that the man did not have a climacteric. There is absolutely no basis for the belief that the man does not have a decrease in sex function in later life, and that he cannot have a climacteric. The climacteric does not necessarily preclude the possibility of sexual relationship, but there is a decline in libido and the ability in the man to have coitus as frequently as in earlier life. This also applies to women of climacteric age who have no more sex potency than have men of the same age; the seeming difference is only that of anatomic structure.

The author is inclined to believe, from clinical experience with male patients, that practically as many men as women experience some degree of glandular disturbance with characteristic symptoms, if the condition were recognized and provided that correct information were available.

The climacteric usually occurs later in men than in women. The average age of onset in women is about 40.8 years, and in men it occurs from approximately 45 to 55, or even 60 years of age.[12-15] It must be remembered that neither the man nor the woman need to be of climacteric age to develop the typical climacteric symptoms. If at any time after the onset of gonadal function, there is a marked decrease of this function, regardless of age, the person is liable to develop the climacteric symptoms.

Decreased gonadal function in men may be primary or secondary. In primary insufficiency of the testicles, normally placed testes have never functioned to a normal degree. Second-

TABLE 6

FREQUENCY OF NERVOUS SYMPTOMS IN THE MALE CLIMACTERIC

	Per Cent
Nervousness, subjective	90.5
Irritability	80.2
Excitability	49.0
Depression	77.2
Crying	15.3
Memory and concentration decreased	75.8
Loss of interest	55.8
Decrease in self confidence	27.1
Ill at ease	56.4
Fear of impending danger	40.6
Worry, unnecessary	33.7
Personality change, unsociable, desire to avoid crowds and company	23.8
Self accusatory	2.4
Feeling of futility	27.1
Thoughts of self destruction	7.4
Suicide attempted (2 persons)	
Psychoses (9 patients)	2.4
Sleep disturbed	59.3
Occipitocervical aching	41.9
Vertex pressure	17.5
Headache	31.8
Itching	31.8
Formication	20.5

TABLE 7

FREQUENCY OF GENERAL SYMPTOMS AND SIGNS IN THE MALE CLIMACTERIC

	Per Cent
Fatigability and lassitude	80.2
Libido (data on 252 patients)	
Decreased or absent	
Yes	80.5
No	19.5
Potency (data on 263 patients)	
Decreased or absent	
Yes	90.1
No	9.9
Vague pains	32.9
Constipation	24.9
Obesity (moderate)	21.5
Social status:	Number
Single	42
Married	192
Widowed	19
Divorced	20
	Years
Average age of all patients	50.5
Average age of climacteric patients	53.7
Average age of hypogonadal cryptorchidic and eunuchoid patients	33.1

TABLE 8

THE MALE CLIMACTERIC SYNDROME: ORDER OF FREQUENCY OF SYMPTOMS IN TWO HUNDRED AND SEVENTY-THREE PATIENTS

		Per Cent
1.	Nervousness, subjective	90.5
2.	Potency decreased or absent	90.1
3.	Libido decreased or absent	80.5
4.	Irritability	80.2
5.	Fatigability and lassitude	80.2
6.	Depression	77.2
7.	Memory and concentration decreased	75.8
8.	Sleep disturbed	59.3
9.	Loss of interest	58.5
10.	Ill at ease	56.4
11.	Tachycardia, palpitation and dyspnea	51.2
12.	Excitability	49.0
13.	Vertigo	46.5
14.	Numbness and tingling	43.9
15.	Occipitocervical aching	41.9
16.	Fear	40.6
17.	Worry, unnecessary	33.7
18.	Cold hands and feet	32.9
19.	Vague pains	32.9
20.	Headache	31.8
21.	Itching	31.8
22.	Hot flushes	29.3
23.	Loss of self confidence	27.1
24.	Futility	27.1
25.	Scotomas	26.0
26.	Constipation	24.9
27.	Unsociability	23.8
28.	Obesity	21.5
29.	Aching in the vertex	17.5
30.	Sweating	17.9
31.	Crying	15.3
32.	Tinnitus	10.6
33.	Thoughts of self destruction	7.4
34.	Chilly sensations	6.2
35.	Self accusatory	2.4
36.	Psychosis	2.4
37.	Suicide attempted (2 patients)	

ary decreased function of the testes occurs when these glands apparently have functioned normally and later there is a decrease in their secretory activity.

Secondary failure to function normally may occur at any time during the period of active sexual life of the individual and it may result from insufficient stimulation of the testicles by the pituitary gland, or failure of adequate response of the testicles to normal stimulation by the pituitary. The testicles may be subject to decreased function following toxic conditions, infections, and various other ailments. Insufficient function of the thyroid gland is sometimes responsible for hypofunction of the testicles, by failure to stimulate normal chemical cellular activity of all body structures, including the testes.

Complete or partial loss of function of the testicles can also occur from any of the following conditions, namely, castration or bilateral inflammation of the testicles from any cause especially mumps, or following opera-

tions for hernia, if the circulation to the testicles is markedly impaired. X-ray radiation of the male genital organs in the region of the testicles may injure these glands so that they will lose their function, if they are not properly protected. In some instances it is necessary to use the x-ray for treatment, as in malignant conditions.

If any of these harmful conditions occur after the patient has had normal gonadal function, severe glandular imbalance will result in the appearance of the symptoms characteristic of the climacteric and these symptoms may persist with varying intensity until the time for the individual to develop a normal postclimacteric endocrine balance, which may be an indefinite number of years.

After a man has developed normally and functioned sexually, and then has hypofunction or afunction at some later date, the diagnostic evidence for the condition is chiefly subjective, rather than objective. The symptoms result from functional imbalance between the pituitary and the testes (the thyroid and adrenal glands may be secondarily involved), with disturbance of the autonomic and central nervous systems. The symptoms are necessarily chiefly functional. (Tables 5 to 8.)

The author made diagnostic surveys of 273 male patients, each of whom had one of the types of testicular underactivity. Of these patients, 230 were in the climacteric, while the remainder of the patients had hypofunction or afunction, due to failure of normal development or conditions which destroyed testicular function.

Most of these patients complained of symptoms similar in every detail to those found in the female climacteric. Nervousness, poor sleep, easy fatigue, and irritation were all found among the males. The characteristic vertex and occipital headaches, decreased concentration, and mood changes even to melancholia were significant at this time.

Men have hot flushes similar to women. Vertigo, tinnitus, lassitude, and fatigue are often present. Most of these men have noticed a decrease in sexual potency, and in many instances the decline of potency and the persistence of libido causes many men to consult the physician.

The great majority of these patients volunteered the information, that decrease of libido and potency, with few exceptions, were not their chief concern. They were more interested in having relief of their symptoms, especially those which were nervous and psychic; they wanted to feel well, so that they could work. One can almost surely promise a climacteric patient relief from his symptoms and a feeling of well-being, by treatment with the proper dosages of testosterone.

REFERENCES

1. Werner, August A.: Syndrome accompanying ovarian hypofunction. J. Missouri M. A. 28:363-369, 1931.
2. ———: Syndrome accompanying deficiency or absence of ovarian follicular hormone. Endocrinology 19:695-700, 1935.
3. ———: Endocrinology, clinical application and treatment. Ed. 2. Philadelphia, Lea & Febiger, 1942.
4. ———, and Collier, W. D.: The effect of theelin injections on the castrated woman. Proc. Soc. Exper. Biol. & Med. 29:1142 (June) 1932.
5. ———, and ———: The effect of theelin injections on the castrated woman, with histologic report. J.A.M.A. 100:633, 1933.
6. ———, and ———: Production of endometrial growth in castrated woman. J.A.M.A. 101:1466, 1933.
7. ———, Jones, G., Roberts, J., Broun, G. O., Neilson, C. H., and Rothermich, N. O.: Effective clinical dosages of theelin in oil. J.A.M.A. 109:1027, 1937.
8. ———, Johns, G. A., Hoctor, E. F., Ault, C. C., Kohler, L., and Weis, M. W.: Involutional melancholia: probable etiology and treatment. I. J.A.M.A. 103:13-16, 1933.
9. ———, Kohler, L. H., Ault, C. C., and Hoctor, E. F.: Involutional melancholia, probable etiology and treatment, II. Arch. Neurol. & Psychiat. 35:1076, 1936.
10. Ault, C. C., Hoctor, E. F., and Werner, A. A.: Theelin therapy in the psychoses. J.A.M.A. 109:1786, 1937.
11. Werner, A. A., Hoctor, E. F., and Ault, C. C.: Involutional melancholia, a review with additional cases. Arch. Neurol. & Psychiat. 45:944, 1941.
12. Werner, August A.: The male climacteric. J.A.M.A. 112: 1441-1443 (April 15) 1939.
13. ———: The male climacteric; additional observations of thirty-seven patients. J. Urol. 49 (June) 1942.
14. ———: The male climacteric; report of fifty-four cases. J.A.M.A. 127:705-710 (March 24) 1945.
15. ———: The male climacteric; report of two hundred seventy-three cases. J.A.M.A. 132:188 (September) 1946.

The Treatment of Prostatic Cancer

REED M. NESBIT*

UNIVERSITY OF MICHIGAN MEDICAL SCHOOL, ANN ARBOR

Never before during recorded history has man enjoyed such longevity as at the present time. At the turn of the century the life expectancy in our country was 47 years; today it is 20 years greater; but with this remarkable lengthening of life there has been a corresponding increase in the number of deaths due to cancer. Today there are about 17 million males in this country who are over 50 years of age—and about 20 per cent of them have cancer of the prostate. These 3 or 4 million men will not all die of the disease, but many will; and the high incidence of this malignancy constitutes a matter of grave concern for all physicians who are charged with the responsibility of caring for middle-aged or old men.

We do not know why this neoplasm develops, but its occurrence is thought to depend upon testicular function, for eunuchs have not been known to develop it. Some investigators believe that prostatic cancer develops in conjunction with benign hypertrophy and conclude that the two conditions have a common etiologic background. But the investigations of Moore and others tend to contradict this viewpoint, for they have shown that the incidence of prostatic malignancy is as great among men with otherwise normal glands as it is among those afflicted with benign hypertrophy; and Ravisch has shown that Jews display a remarkable immunity to prostatic carcinoma although benign enlargements do tend to occur commonly among them.

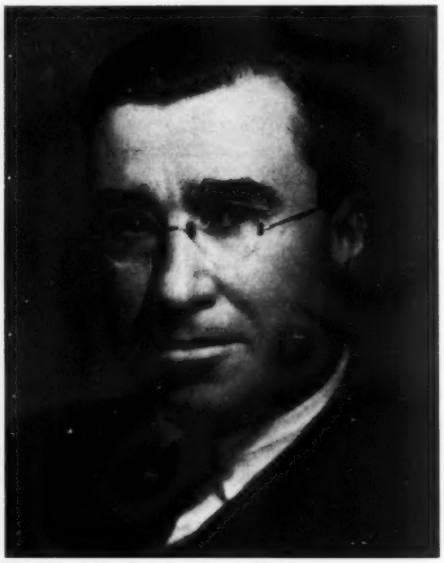
The clinical approach to the problem of prostatic cancer is concerned with three essential enterprises, prevention of the disease, its cure, and palliative or suppressive treatment when it has fully developed.

PREVENTION

In general, the prevention of prostatic cancer is not practically feasible, for nothing short of total prostatectomy can today be regarded as an absolute prophylaxis against the disease. However, total prostatectomy has been recommended for the treatment of many nonmalignant conditions today, and those urologists who routinely perform perineal prostatectomy in the treatment of benign enlargements might logically advocate total prostatectomy whenever the perineal approach is indicated, thus

*Department of Surgery, University of Michigan Hospital, Ann Arbor.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.



REED M. NESBIT

adding the benefit of cancer prevention to the other advantages inherent in the perineal operation. But total prostatectomy is invariably followed by complete sexual impotence and many individuals who suffer from prostatism would be unwilling to exchange their remaining sexual powers for prevention of cancer if they knew that 4 out of 5 persons do not develop the disease anyway.

CURE

CURE of prostatic cancer can be accomplished only by radical perineal prostatectomy that is performed while the lesion is sharply localized. Every man who is found to have an area of induration in the prostate should be afforded the benefit of perineal exposure of the prostate so that frozen section biopsy can be performed, and early radical removal of the gland carried out if malignancy is present. Only in this way can cure of prostatic cancer be effected.

Most women today have been educated to the importance of periodic examinations of the breasts, but the male population in general is totally ignorant about the dangers of prostatic cancer, or of the need of periodic rectal examinations. Most early prostatic cancers are discovered not by urologists but by conscientious practitioners. Radical perineal prostatectomy is not a difficult operation to perform and it is a safe operation. Hinman has recently stated that five-year cures can be expected in at least 50 per cent of the cases. A recent review of the data relating to the patients who have been treated for cancer of the prostate in the University of Michigan Hospital since 1925 reveals the interesting fact that all of the patients who had radical perineal prostatectomy survived operation, all enjoy urinary continence, and all are alive today. But only 5 per cent of prostatic cancers are discovered early enough to permit the employment of radical surgery, a lamentable and dismally low figure considering the fact that most of the lesions could be recognized early if only an early rectal examination were made.

PALLIATIVE TREATMENT

The palliative or suppressive endocrine treatment of prostatic cancers which cannot be removed by radical surgery commenced in 1941 following the epoch-making discoveries of Charles Huggins, who in that year demonstrated a functional relationship between this disease and certain hormones. Since that time physicians have treated patients suffering from carcinoma of the prostate by the administration of estrogenic hormones and by surgical castration. The series of cases that are being reported currently from many clinics will doubtless provide a means for final evaluation of the methods that are being employed. Spectacular regression of the primary neoplasm has been observed in many of the patients, and, in some instances, complete disappearance of metastases has occurred. Some of the patients, however, have shown improvement for a short time only and a few have apparently derived no benefit

whatever from the endocrine modifications employed.

We have been following two closed series of cases at the University of Michigan Hospital since 1941. One of the series is composed of 75 patients who were treated by castration, while the other consisted of 50 cases treated by estrogens alone. At the present time these two series have been followed for approximately five and one-half years, and the survival rates shown in Table I have recently been tabulated for comparison.

TABLE 1
SURVIVAL RATES TO JULY 1947 (CLOSED SERIES)

	ORCHIECTOMY SERIES (75 CASES)	STILBESTROL SERIES (50 CASES)
Alive and symptom-free	22.7 per cent	18.0 per cent
Dead or recurrence of symptoms	78.3 per cent	82 per cent

These data suggest that the over-all survival rates in the two series are approximately the same. They also demonstrate that neither form of treatment offers assurance of prolonged remission, a fact that should be borne in mind in determining the most suitable time to inaugurate endocrine therapy. Added information on the latter point is afforded by the survival data (Table 2) on the patients who had cancer without metastases at the time that treatment was initiated.

TABLE 2
SURVIVAL RATES OF PATIENTS WITHOUT METASTASES (CLOSED SERIES)

	ORCHIECTOMY SERIES (45 CASES)	STILBESTROL SERIES (33 CASES)
Alive and symptom-free	29 per cent	27.2 per cent
Dead or recurrence of symptoms	71 per cent	72.8 per cent

It is evident that neither form of therapy affords prophylaxis in the prevention of metastases or advance of the disease, and reason would seem to dictate that endocrine therapy be regarded as a palliative measure only, and for that reason it should be employed only in advanced stages of the disease.

TABLE 3
SURVIVAL RATES OF PATIENTS WITH METASTASES (CLOSED SERIES)

	ORCHIECTOMY SERIES (30 CASES)	STILBESTROL SERIES (17 CASES)
Alive and symptom-free	13.3 per cent	0 per cent
Dead or recurrence of symptoms	86.6 per cent	100 per cent

Many questions have arisen concerning the relative merits of the two methods of endocrine therapy that are under discussion. Huggins has steadfastly contended that castration is complete, and that its effects are continuous; but other observers have favored estrogen therapy in the view that this hormone neutralizes not only the testicular hormone, but also other hormones which might stimulate the growth of the tumor.

One obvious and practical disadvantage to estrogen therapy is the ever-present human attribute of forgetfulness and neglect. One-fifth of the patients in our estrogen series forgot or failed to take their pills regularly; and at least two of the patients stopped taking the hormone altogether, after having gone into a remission, in the belief that the cancer had been cured! Another disadvantage in the method of using estrogens is some of the patients who failed to respond satisfactorily to estrogen therapy have had remissions following castration, but none of the castration failures have been improved by estrogen therapy.

Additional evidence in the comparison of the two methods of endocrine therapy is afforded by the survival data on patients who had demonstrable metastases at the time treatment was begun (Table 3).

In Table 3 it would appear that orchiectomy is more effective than estrogen therapy as a palliative measure in those patients with metastasis. However, when the data are subjected to statistical analysis (Chi-Square formula and Yates' correction), it is found that the differences between the orchiectomy series and the

stilbestrol series are not statistically significant at the 5 per cent level in either table. That means that such differences might be expected to arise by chance more often than five times in a hundred and we can therefore make no statistical statement regarding the superiority of one treatment over the other, other factors being equal. More time is necessary and larger series of cases must be critically analyzed before final evaluations can be made, but the present series permits the inference that castration provides better clinical response than estrogen therapy alone.

CONCLUSIONS

Cancer of the prostate can be cured by early recognition and radical perineal prostatectomy, but it is to be deplored that only 5 per cent of the cases are recognized early enough to permit the operation.

Endocrine therapy is a palliative measure that is best reserved until the advanced stages of the disease have developed, and the evidence that has been presented suggests that castration may be more effective than estrogen therapy alone in producing remissions in patients suffering from advanced cancer of the prostate.

NEW FILM ON MANAGEMENT OF FAILING HEART

After two years of preparation, announcement has been made of the completion of a new sound and color film entitled "Management of the Failing Heart." The new forty minute length film is available to medical groups throughout the country.

A modern regimen for the treatment of congestive heart failure is narrated and depicted. Animated charts and diagrams, clinical sequences, and pathologic specimens are used to visualize the five essential steps necessary in the management of the failing heart, viz., (1) rest, (2) diuretics, (3) salt-free diet, (4) liquid intake, and (5) digitalization.

The film thoroughly airs the controversial subject of the nature of "rest," and goes into great detail regarding control of cardiac edema through a better understanding of the proper use of mercurial diuretics, the role of salt in the cardiac diet, and the subject of a liberal water intake.

The physician is shown the efficacy of the average single dose method of digitalization and simplified maintenance by the use of the purified digitalis glycoside, Digitaline Nativelle. This is demonstrated by electrocardiograms and case history charts.

The film was prepared from a text supplied by and with the cooperation of the Department of Pharmacology, Cornell University Medical School, under a grant established by Varick Pharmacal Company, Inc.

The Present Status of Antibiotic Therapy

JOHN A. KOLMER*

TEMPLE UNIVERSITY SCHOOL OF MEDICINE, PHILADELPHIA

While a large number of antibiotic agents has been produced, only penicillin, streptomycin, tyrothricin, and bacitracin are being employed at the present time for prophylaxis and treatment of disease.

Crystalline sodium G and crystalline potassium G penicillins are preferred. As dispensed in a dry state, both are highly stable at ordinary temperatures while being less toxic and less irritating than amorphous products. Solutions, however, should be kept in a refrigerator. Streptomycin is dispensed as sulfate and hydrochloride salts of the compound; also as a calcium chloride complex which, in a dry state, is highly stable at ordinary temperatures. Solutions of streptomycin, however, should likewise be kept at a low temperature.

NATURAL RESISTANCE OF BACTERIA

Different strains of any bacterium susceptible to penicillin may possess a high natural resistance to the compound. Thus, streptococci of the viridans type and anaerobic streptococci are usually much more resistant than beta hemolytic streptococci of group A; staphylococci also vary greatly in natural resistance.

The same is true of streptomycin. Thus, some strains of *Escherichia coli* and other gram-negative bacilli may be much more resistant than usual. This has an important bearing on dosage and administration and may be responsible for treatment failures. Fortunately, however, gonococci and other organisms naturally resistant to the sulfonamide compounds are usually highly susceptible to penicillin.

Sometimes streptococci, staphylococci, and other gram-positive organisms may be found less naturally resistant to streptomycin than to penicillin *in vitro,* with the suggestion that the former may be preferred in treatment.

ACQUIRED RESISTANCE OF BACTERIA

Bacteria may also show so-called acquired resistance to penicillin or streptomycin during treatment which, likewise, has an important bearing on dosage and method of administration. This happens much more rapidly and frequently to streptomycin than to penicillin.

True acquired resistance of bacteria to these compounds, however, may not actually occur but only represent the survival or emergence

*Professor of Medicine, Temple University School of Medicine and School of Dentistry; Director, Research Institute of Cutaneous Medicine, Philadelphia.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

JOHN A. KOLMER

of naturally resistant variants of any given bacterium during treatment. In other words, these compounds may rapidly reduce or eliminate highly susceptible organisms, leaving more naturally resistant variants which are thought to be organisms of so-called acquired resistance.

Under the circumstances penicillin and streptomycin should not be used indiscriminately in the prophylaxis and treatment of disease since the survival of naturally resistant variants is of epidemiologic importance.

SYNERGISTIC OR ADDITIVE CHEMOTHERAPY

Synergistic or additive chemotherapy consists of the administration of two compounds conjointly and especially in the treatment of severe infections, including mixed infections. In some instances the therapeutic effects appear to be truly synergistic while in others, they are merely additive.

Since penicillin and streptomycin are of very low toxicity, untoward or toxic reactions are usually no greater and may be less since smaller doses of each compound may be employed than of either alone. Furthermore, this combined therapy may prevent or reduce the incidence of so-called acquired resistance of infecting organisms.

Excellent results have been observed in the treatment of various experimental infections, like syphilis of rabbits, with penicillin, mapharsen, or bismuth; tuberculosis of guinea pigs and rats with streptomycin and the sulfone compounds; streptococcal, pneumococcal, and typhoidal infections of mice with penicillin and sulfonamide compounds; *Klebsiella pneumoniae* infections of mice with streptomycin and sulfadiazine, and anthrax of mice with penicillin and streptomycin.[1, 2, 3]

Consequently, this combined chemotherapy is frequently indicated in the treatment of the septicemias, acute bacterial endocarditides, suppurative meningitides, bronchiectasis, pneumonias, suppurative pneumonitides, sinusitis, suppurative arthritides and compound fractures, osteomyelitis, brain abscesses, carbuncles, Ludwig's angina, erysipelas, gangrene, actinomycosis, gonorrhea and its complications, and other diseases with penicillin or streptomycin and the sulfonamide compounds. It is also worthy of clinical trial in the treatment of syphilis, especially early syphilis, with penicillin, mapharsen, or bismuth as well as in the treatment of tuberculosis with streptomycin and sulfone compounds, with particular reference to promizole.

PRINCIPLES OF ANTIBIOTIC THERAPY

Whenever possible, accurate bacteriologic diagnosis is always advisable in relation to penicillin and streptomycin therapy since the administration of these compounds is indicated only in the treatment of pure or mixed infections due to susceptible organisms. In many instances, however, the physician or surgeon is justified in making a presumptive clinical diagnosis and proceeding with penicillin or streptomycin therapy without delay.

Laboratory tests for determining the susceptibility of organisms to penicillin or streptomycin *in vitro* are also frequently advisable or necessary as a clinical guide to dosage and administration, since infections due to strains with high natural or so-called acquired resistance require larger doses and more prolonged treatment than infections due to highly susceptible organisms.

Assays of the blood, spinal, and other body fluids for penicillin or streptomycin are likewise frequently necessary or advisable at intervals during treatment as a guide to dosage and route of administration. Effective concentrations of penicillin in the serum should be within the limits of 0.02 to 2 or more units, with a general average of about 0.15 units per cc., while effective concentrations of streptomycin vary from about 2 to 20 micrograms (units) per cc. or higher, according to the nature and severity of the infection. Otherwise, and when in doubt, dosage and methods of administration of these compounds must be based upon clinical judgment and experience alone.

Treatment should always be instituted as soon as possible and especially in acute infectious diseases in which large doses over a short period of time are to be preferred to small doses over a long period.

There are practically no contraindications to penicillin or streptomycin therapy of diseases due to susceptible organisms, except in patients possessing a high degree of natural or acquired allergic sensitization to the compounds. Under these circumstances due caution is required in dosage and administration or treatment abandoned.

Penicillin or streptomycin therapy alone is not always a substitute for adjuvant measures of sound therapeutic value, with special reference to prompt drainage or other surgical measures, blood transfusions, the administration of specific immune sera, etc., and particularly in the treatment of severe infections. Indeed, neither compound is incompatible with any drug, x-ray, or any other kind of therapy of proved or helpful value, including induced fever employed in the treatment of gonorrhea, syphilis, etc., which appears to enhance the therapeutic activity of chemotherapeutic compounds.

CAUSES OF TREATMENT FAILURES

Treatment failures may be due to any of many causes among which may be mentioned: (1) mistaken clinical or bacteriologic diagnoses; (2) infections due to organisms possessing a high natural or so-called acquired resistance to penicillin or streptomycin; (3) doses too small, intervals of administration too long, or duration of treatment too brief; (4) overwhelmingly severe infections or too long delay in the institution of treatment; (5) localization of infections in areas inaccessible to penicillin or streptomycin; (6) inadequate surgical treatment or failure to use other adjuvant measures of helpful value, and (7) the occurrence of spontaneous new infections or superinfections with other organisms indicating the frequent need for repeated bacteriologic examinations during treatment.[4]

DOSAGE AND ADMINISTRATION OF PENICILLIN AND STREPTOMYCIN

The dosage of penicillin and streptomycin varies from one patient to another, depending not only on the nature, severity, and location of the infection, but on age, weight, the presence or absence of septicemia, and *especially susceptibility of the infecting organism to the compound.*

Consequently, the physician or surgeon should not depend on "average doses." Treatment should be individualized, especially in severe infections, since blind adherence to average doses may result in therapeutic failures. Rather, dosage should be such as to secure and maintain blood concentrations at least 2 to 5 times higher than those to which the infecting micro-organism is susceptible *in vitro.* When unfavorable therapeutic results are observed one should redetermine the sensitivity of the organism *in vitro* and the blood concentration, and promptly increase the dosage or

otherwise alter treatment as indicated.

Infections of highly vascularized soft tissues respond to doses which may be ineffective in infections of poorly vascularized and hard tissues like bones and joints; acute and diffuse lesions usually respond more favorably than chronic localized ones.

Maximum doses are always advisable at the beginning of treatment and especially in severe infections. For this purpose penicillin may be administered by continuous intravenous or intramuscular injection and streptomycin by continuous intramuscular injection.

The urinary excretion of penicillin may be reduced with a consequent increase and prolongation of blood concentrations by the oral administration of 2 gm. sodium benzoate or 2 to 4 gm. caronamide every four hours.[5, 6] Sodium benzoate has been found less effective in enhancing the blood concentrations of streptomycin[7] while caronamide has not been reported on in this connection.

Since the duration of treatment is likewise variable, it should be guided not only by clinical judgment but by laboratory examinations whenever possible; it is better to administer too much than too little in order to prevent relapsing infections.

Repeated bacteriologic examinations are advisable for the detection and treatment of spontaneous new infections and especially with organisms normally present in the nasopharynx.[4]

In case of necessity the laity may be trained to give intermittent intramuscular injections of penicillin or streptomycin dissolved in sterile saline solution.

Penicillin should not be given orally in the treatment of severe staphylococcal infections, subacute bacterial endocarditis, all types of meningitis, and syphilis.

THERAPEUTIC VALUE OF PENICILLIN

Penicillin, with or without synergistic or adjuvant therapy, has usually proved highly effective in the treatment of various and diverse staphylococcal, streptococcal, pneumococcal, meningococcal, gonococcal, and clostridial infections including postoperative bacterial synergistic gangrene. It has also proved effective in the treatment of anthrax, erysipeloid and Haverhill fever, syphilis, yaws, spirofusillar infections, and actinomycosis.

In subacute bacterial endocarditis large doses should be given over a period of at least four to eight weeks; coincident anticoagulant therapy with heparin or dicumarol may slightly improve the results but is generally regarded as too hazardous.

In primary syphilis the total dosage should be at least 6,000,000 units and at least 9,000,000 units in early secondary syphilis. In neurosyphilis, concomitant fever therapy should be employed.

Intrathecal injections should always be given at least once or twice daily in suppurative meningitis in conjunction with parenteral injections. Likewise, intrathoracic injections at least once daily in empyema and intraabdominal injections at least once daily in peritonitis with retention of the compound for at least six to eight hours in either case.

Topical applications of penicillin ointment may have to be stopped after five consecutive days because of allergic sensitization, especially in skin diseases.

THERAPEUTIC VALUE OF STREPTOMYCIN

Streptomycin is usually highly effective in treatment of tularemia, the septicemias, endocarditides, meningitides, pneumonias, and unobstructed urinary tract infections due to the pathogenic *gram-negative bacilli.*

It is of helpful or variable value in the treatment of empyema, peritonitis, liver abscess, cholangitis, wounds, burns, and compound fractures due to infections with gram-negative bacilli. Streptomycin is also of value as a suppressive agent in the treatment of exudative pulmonary tuberculosis, in tuberculous laryngitis, meningitis, peritonitis, fistulae, osteomyelitis, and arthritis, but usually ineffective in the treatment of tuberculous empyema. The compound, however, is of but doubtful value or disappointing in the treatment of acute

brucellosis, typhoid fever, paratyphoid fever, and other Salmonella infections.

Intrathecal injections of 50 to 100 mg. daily or every other day, are essential in addition to intramuscular injections in the treatment of meningitis; also intrathoracic or intraabdominal injections of 0.5 to 1.0 gm. with retention for six to eight hours in the treatment of empyema and peritonitis.

Oral administration is indicated only in preoperative preparation for intestinal surgery. Aerosols may be employed. Suspensions in peanut oil and beeswax are probably ineffective.[8]

PROPHYLACTIC APPLICATIONS OF PENICILLIN

Undoubtedly penicillin has proved of value in prophylaxis of infections by susceptible organisms. Intermittent intramuscular injections of aqueous solutions or P.O.B. (suspensions in peanut oil and beeswax) are usually to be preferred. Oral administration, however, may suffice for the prevention of minor infections; likewise, local applications of 5,000 units per gram sulfonamide crystals in postoperative wounds. As a prophylactic measure against infection after surgical or obstetric operations and manipulations, intramuscular injections should be started two or more days before and continued for a variable time thereafter.

Penicillin may be used advantageously in the prevention of (1) infection in traumatic or postoperative wounds and compound fractures; (2) empyema following lung resection; (3) gaseous gangrene following amputations; (4) infection of skin grafts; (5) ocular infections after penetrating injuries, burns, etc.; (6) ophthalmia neonatorum; (7) puerperal infection following abortion or severe dystocia; (8) septicemia following surgical operation or manipulation in osteomyelitis; (9) intracranial infections following operations on the mastoids or sinuses; (10) peritonitis after rupture of the appendix, abdominal wounds, etc.; (11) infection following perforating wounds of the hands or feet; (12) subacute bacterial endocarditis after extractions of teeth, tonsillectomy, etc.; (13) for the prevention of scarlet fever and streptococcal throat infections in rheumatic carditis, and (14) for the prevention of congenital syphilis by treatment during pregnancy.

THERAPEUTIC APPLICATIONS OF TYROTHRICIN

Tyrothricin is a mixture of gramicidin and tyrocidine produced by *Bacillus brevis*. It is highly active against staphylococci, streptococci, pneumococci, *N. catarrhalis, Lactobacillus acidophilus* and mouth spirochetes. It is dispensed as a 2 per cent solution in alcohol and in ointments.

This compound, however, is too hemolytic and otherwise toxic for parenteral administration and is relatively ineffective by oral administration. Consequently it is used only by topical application. A 1:5000 colloidal suspension in *sterile water* (0.2 mg. per cc.) is usually well borne (1 cc. of alcoholic solution in 100 cc. of water).

Tyrothricin is worthy of trial in the prevention and treatment of surface infections by gram-positive organisms including wounds, burns, skin grafts, osteomyelitis, postoperative sinuses, chronic ulcers, sinusitis, mastoiditis, purulent rhinitis, otitis media, empyema, cystitis, suppurative arthritis, ophthalmic infections, furuncles, carbuncles, eczematoid dermatitis, and others.

BACITRACIN

Bacitracin is a new antibiotic agent produced by a member of the *Bacillus subtilis* group.[9] It has been found highly active against gram-positive organisms, especially streptococci and staphylococci, and its bactericidal activity is stated not to be materially reduced by plasma, blood, pus, and tissue products.

Bacitracin has been employed only in the treatment of local infections by injections of aqueous solutions into lesions (0.1 to 5.0 cc. carrying 100 units), by topical applications of aqueous solutions, or by applications of ointment prepared in a water-soluble base.[10]

Its therapeutic value cannot be stated at the present time but it may prove of value in the

treatment of local infections due to gram-positive organisms resistant to penicillin, like furuncles and other abscesses, carbuncles, infected wounds, ulcers, impetigo, etc.

REFERENCES

1. Callomon, F. T., Kolmer, J. A., Rule, A. M., and Paul, A. J.: Streptomycin and diasone in the treatment of experimental tuberculosis of guinea pigs. Proc. Soc. Exper. Biol. & Med. 63:237, 1946.
2. Kolmer, J. A., and Rule, A. M.: Penicillin in the treatment of experimental syphilis of rabbits: II. The synergistic or additive activity of penicillin, oxophenarsine hydrochloride and bismuth and potassium tartrate. Arch. Dermat. & Syph. 56:179, 1947.
3. Kolmer, J. A.: The synergistic or additive activity of chemotherapeutic compounds. Am. J. M. Sc. (In press.)
4. Weinstein, L.: The spontaneous occurrence of new bacterial infections during the course of treatment with streptomycin or penicillin. Am. J. M. Sc. 214:56, 1947.
5. Seeler, A. O., Wilcox, C., and Finland, M.: Enhancement of blood levels by caronamide during intramuscular administration of penicillin. J. Lab. & Clin. Med. 32:807, 1947.
6. Strauss, E., Richburg, P. L., Saba, P. Z., and Alexander, J. E.: Enhancement of plasma penicillin concentrations by caronamide and sodium benzoate. J. Lab. & Clin. Med. 32:818, 1947.
7. Kolmer, J. A., Bondi, A., Warner, H. F., and Dietz, C.: Influence of sodium benzoate by ingestion upon urinary excretion of streptomycin. Proc. Soc. Exper. Biol. & Med. 63:455, 1946.
8. Kolmer, J. A., Bondi, A., Warner, H. F., and Dietz, C.: Administration of streptomycin in peanut oil and beeswax and in solvecillin. Science 104:315, 1946.
9. Johnson, A. B., Anker, H., and Meleney, F. L.: Bacitracin: a new antibiotic produced by a member of the B. subtilis group. Science 102:376, 1945.
10. Meleny, F. L., and Johnson, B.: Bacitracin therapy: the first hundred cases of surgical infections treated locally with the antibiotic. J.A.M.A. 133:675, 1947.

BETTER DRUG SOUGHT FOR CHILDBIRTH PAINS

To relieve the pains of childbirth, with safety to mother and child, American chemists have been challenged to produce a new drug better than any now available.

Drug manufacturers were asked to aid in this search by Dr. Bert B. Hershenson of the Boston Lying-In Hospital at the newer analgesics conference of the New York Academy of Sciences.

Specifically, Dr. Hershenson wants a drug that has the advantages without the disadvantages of scopolamine, known to the lay public as the "twilight sleep" producer. This drug, used with apomorphine, is still the best there is for safe pain relief for the woman in labor, Dr. Hershenson and associates believe. Their opinion is based on experiences at their hospital that go back for more than a century.

DIAGNOSTIC CLINIC

Surgery of the Pancreas

RICHARD B. CATTELL*

LAHEY CLINIC, BOSTON

Diseases of the pancreas offer many difficulties in diagnosis and, above all, considerable technical difficulties in carrying out curative operative procedures. We have a relatively new field of surgery in the consideration of surgery for pancreatic diseases. For many years there have been sporadic attempts at the elimination of tumors, and many operative procedures for the more common inflammatory diseases involving the pancreas. Except for the catastrophe of acute pancreatitis, the symptoms of pancreatic disease are obscure. Furthermore, we do not have the aids that we have in other surgical diseases, since special studies and special diagnostic aids are of little value in establishing the diagnosis.

The diagnosis of pancreatic disease is usually made by exclusion. In other words, many of the common disorders of the gastrointestinal tract, the kidney, and the retroperitoneal region are first investigated, and when no diagnosis can be established, we then think of this blind area occupied by the pancreas.

Surgical diseases of the pancreas can be divided into three general groups:

1. Those of inflammatory origin. This classification will include the fairly common acute pancreatitis; the less common and little understood chronic pancreatitis—chronic relapsing pancreatitis—which produces marked changes in the gland both structurally and functionally; cysts, many of which are of inflammatory origin; fistulas, either of inflammatory origin or from trauma, and finally calcification or pancreatolithiasis.

2. Congenital disorders, of which little is known. First are included congenital cysts, since congenital fistulas are not encountered. Second, obstruction to the duodenum or to the ducts of the pancreas as a result of developmental failure.

3. Finally, we have a subject which interests us particularly today and has done so during the past twelve years—tumors of the pancreas, which include the benign or hyperfunctioning adenomas and, second, carcinoma.

The symptoms of pancreatic disease are somewhat obscure. These again may be divided into three general groups: (1) those that affect the body mechanism and functions as a whole; general symptoms, which might be weakness, loss of weight, and anemia; (2) those of digestive origin that are chiefly due to interference with the passage of the pancreatic ferments into the intestinal tract, indigestion, anorexia

*Department of Surgery, The Lahey Clinic, Boston, Massachusetts.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

RICHARD B. CATTELL

and bowel changes which may be either constipation or diarrhea, and (3) local symptoms, those that are caused by pressure with the presence or absence of pain.

The diagnostic aids available in attempting to establish a diagnosis of surgical disease of the pancreas first include, of course, roentgenologic studies. These again are part of the exclusion of other causes for the symptoms. In studying the patient, the upper gastrointestinal tract, stomach, and duodenum are fluoroscoped, with particular emphasis on a change in the distance between the first portion of the duodenum and the third, the so-called duodenal angle or sweep; second, elimination of colon disorders; lastly, studies of kidney abnormality.

Since the stool is obviously changed as pancreatic ferments are kept from entering the intestinal tract, we see changes in the character of the stool based on incomplete digestion, on increase in the amount of unbroken protein, the increase in fat, etc.

There are two laboratory tests that may be of value. First is a determination of ferments within the blood stream, particularly the serum amylase; and second, the alkaline phosphatase.

Let us consider some of these disorders, how the diagnosis is made, and how these patients are treated.

Pancreatic cysts are somewhat rare. Their pathogenesis can be on more than one basis. They may originate from acute pancreatitis, as, for example, a case that I should like to present to you briefly. The patient was a young man of 32 who had acute pancreatitis; he was operated on, with drainage of his pancreas in May 1942. In March 1943 a mass developed in the abdomen; for several weeks previously he had had recurrent attacks of epigastric pain. He was again operated on one year after the first operation and a large cyst was found which was marsupialized or attached to the skin so that it would drain to the outside and contract.

This resulted in a pancreatic fistula. In June 1944, approximately another year later, this pancreatic fistula was excised. It remained closed for a period of a few months and again the same type of attacks developed. He was operated on again in an attempt to do a partial pancreatectomy, but because of the inflammation that was present, this was not feasible technically. Finally, because of morphine addiction and recurrence of attacks, another operative procedure was done which was relatively new, although it was done by Fontaine and Leriche some years ago, and has been reported recently by Smithwick and by White.

A thoracolumbar sympathectomy was done to relieve the pain. I should like to call this to your attention as a means of relief of visceral pain in the region of the pancreas, since we have now had a number of cases in which it has been effective. This is an indirect approach to the treatment of pancreatic disease, but it may suffice to enable us to get rid of morphine addiction in these patients.

This man had a bilateral splanchnicectomy from the fifth thoracic through the second lumbar, and since that time he has been markedly benefited as far as relief of pain is concerned. In order to carry him along nutritionally, it is necessary to give him large amounts of pancreatic ferment in the form of pancreatin

in order to keep his digestive apparatus working satisfactorily.

The diagnosis of pancreatic cyst will usually be established not by the presence of pain but by symptomless tumor of the upper abdomen. This tumor is localized in the pancreas by the means already outlined, by demonstrating that it is not in the kidneys, spleen, or gastrointestinal tract.

Marsupialization of one of these cysts probably should be done in those cases in which the cyst communicates with the duct system or the duct of Wirsung of the pancreas. Complete excision of the cyst is the best treatment, but it may be necessary to remove the body and tail to accomplish this. This is a difficult technical procedure and I should like to warn against the very close proximity of the inferior mesenteric artery as well as the superior mesenteric artery. It is best to begin the procedure by removing the spleen and lifting up the tail and body of the pancreas from its position in front of the kidney.

A condition in which surgical approach has been tried more recently is that of pancreatolithiasis or calcinosis of the pancreas. The pathogenesis of this disease has but two factors which are known at present. The first is recurrent inflammatory disease of the pancreas; the second factor is the intake of a large amount of alcohol. Nearly all of these patients have an alcoholic history.

These patients have severe pain in the epigastrium, usually passing into the back. These attacks tend to occur with increasing frequency, and may be associated with marked digestive and nutritional disturbances. Nearly all of the patients have a history of morphine addiction, and diabetes mellitus is usually present.

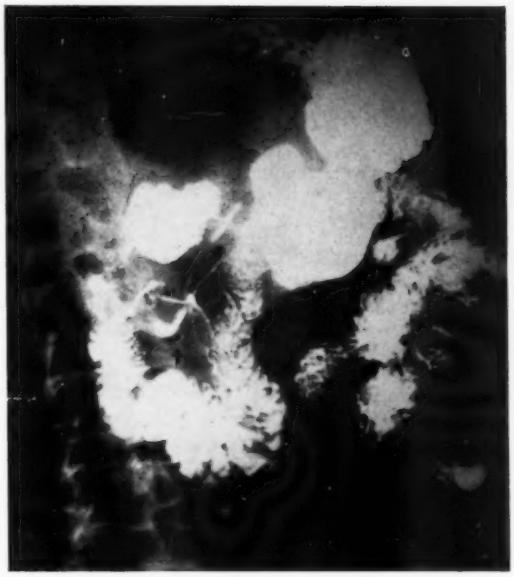


Figure 1. During routine roentgenographic observation of the upper gastrointestinal tract, regurgitation of barium occurred, outlining the pancreatic duct system.

THERE IS very little evidence that can be determined concerning the etiology of acute pancreatitis. Figure 1 is a roentgenogram of a patient who had had repeated bouts of acute pancreatitis and was in a state that might be referred to by Comfort as chronic relapsing pancreatitis. You will see the duct system outlined, the duct of Santorini—the accessory duct in the upper portion of the duodenal sweep—and the communicating main duct system or duct of Wirsung, which shows that this is a cause of the patient's symptoms. The problem of handling the situation in these patients is, of course, an extremely difficult matter.

Rarely do we have the benefit of roentgenologic study such as shown in these cases with or without pancreatolithiasis. In Figure 2 we see deformity of the duodenum, a change in the duodenal sweep, in a patient in whom subsequently the diagnosis of chronic relapsing pancreatitis was confirmed.

In Figure 3 an uncommon finding in patients with recurrent pain of pancreatic origin is illustrated. You will see the presence of many calculi scattered throughout the pancreatic head to the right of the lumbar bodies and also continuing through the rest of the gland.

Figure 2. Deformity of duodenum by an enlarged head of the pancreas due to chronic pancreatitis.

Figure 3. Pancreatolithiasis with stones scattered throughout pancreatic duct system, chiefly concentrated in head. No diffuse calcinosis.

When pancreatolithiasis is present we have a difficult surgical problem to deal with. The best results in this condition, if symptoms are associated with it—they are not always associated with diffuse calcinosis—is a partial pancreatectomy. Particularly if these calculi are scattered through the duct system in the tail and body, partial pancreatectomy will be quite effective.

We have one patient, a woman of 34, who had had recurrent attacks of this type for twelve years. She had lost weight, going from 140 pounds to 110 pounds, and was taking a large quantity of morphine every day. Partial pancreatectomy, including all of the tail, body, and part of the head was accomplished without disengaging the head from the duodenum. In other words, the pancreatic ferments were still left available to the intestinal tract.

After the fifth day following operation she did not have a single dose of morphine nor has she had any difficulty with indigestion, and she has regained her normal weight. Zinninger, Whipple, Waugh, and others have carried out more extensive procedures in similar cases in which the pancreatolithiasis or the diffuse calcinosis extended throughout the remainder of the pancreas. This means total pancreatectomy. It is a procedure fraught with great danger. It is questionable whether we are justified in doing a total pancreatectomy for benign diseases, but further experience will prove whether this point is tenable.

It is interesting to observe from the work reported by these men that the amount of insulin required after total pancreatectomy drops unbelievably low. In other words, after total pancreatectomy perhaps 20 or 30 units of insulin daily is all that is required for these patients.

If on exploration, partial or total pancreatectomy is not feasible, we must resort to the other procedure of sympathectomy. It is probably unnecessary to go as high as the third or fourth thoracic segment to denervate the region of the pancreas, but that has been done in our cases.

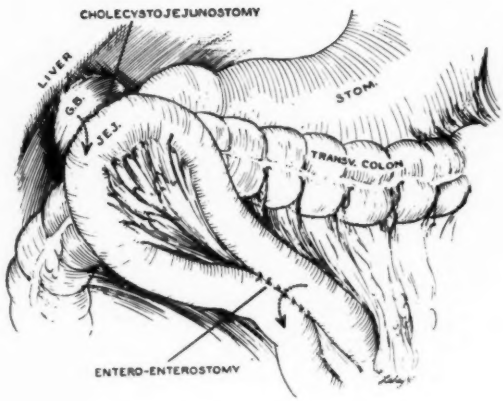


Figure 4. The author recommends this type of first stage operation when two stages are required, antecolic cholecystojejunostomy.

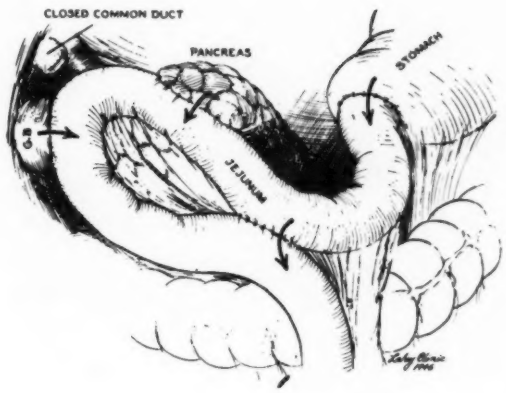


Figure 5. Anastomosis of duct of Wirsung to the jejunum is an essential part of pancreatoduodenal resection. It may be of the open type over a tube, as illustrated, or the closed type, as previously presented by the author.

If most of the pain is rightsided and epigastric, we have been successful in relieving it by sympathectomy on the right side only. In one case, however, in which complete relief of pain was obtained following a right sympathectomy, the patient had pain on his left side after an alcoholic bout and it was necessary to complete the sympathectomy on the other side.

In 1929 the first discrete hyperfunctioning adenoma of the pancreas was reported. Since that time a considerable number has been reported, probably in excess of 250. The first one happened to be malignant. Attention was called to this condition previous to 1929 by Harris, but at the Mayo Clinic, William J. Mayo and his associates reported the first case in 1929.

These patients complain of weakness, fainting attacks, and excessive hunger. They are large consumers of food and frequently awaken at night to take food. This condition may be confused clinically with the petit mal of epilepsy or with carotid sinus syncope. The carotid sinus can be excluded by determining the irritability of the carotid sinus, and the diagnosis can be established only if, during an at-

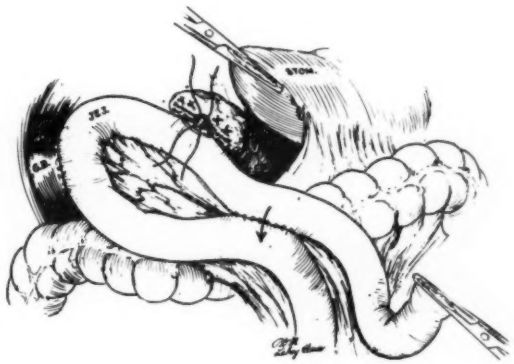


Figure 6. Completed pancreatoduodenal resection, second stage operation, author's method; gastrojejunostomy end-to-end; enteroenterostomy for diversion; pancreatojejunostomy; cholecystojejunostomy, and finally, closure of common duct stump. In the one stage operation the biliary tract anastomosis is choledochojejunostomy.

Figure 7. Postoperative roentgenographic visualization of the upper gastrointestinal tract twelve days after one stage pancreatoduodenal resection.

tack, the blood sugar level is 40 mg. per 100 cc. or below.

The treatment of this condition is obviously excision of the adenoma. Our experience is confined to 9 cases which have been reported by my associates, Drs. Marshall and Allan. It is extremely difficult to locate these small tumors within the pancreas. It is done by division of the gastrocolic omentum, dropping the colon downward, and then searching the entire surface of the pancreas. If the adenoma is not discovered (it may be only a few millimeters in diameter) the pancreas must be freed up and further search made. If this study is unsuccessful, it will be necessary to do partial pancreatectomy.

IMPORTANT advances in surgery of the pancreas have followed the report by Whipple and his associates in 1935 of their work on successful radical removal of carcinoma of the head of the pancreas.

Obviously, if anything is to be accomplished in cancer of the pancreas it can be done only by resection. In a group of 56 consecutive patients operated on before 1935 with the best palliative type of procedure performed—cholecystojejunostomy—75 per cent were dead within six months of their operation or within nine months of their first symptoms. This is a standard to which the comparison of results of resection can be made.

The patient on the platform is a man 67 years of age who was admitted to the hospital in St. Louis on the service of Dr. Elman and Dr. Thomas in May 1947. This man had had symptoms for six months. I would like to call your attention to the importance of bowel symptoms as a possible indication of pancreatic disorder. He had had no passage of blood, but had noticed increasing constipation. Subsequent to this he began to lose his appetite and then had complete distaste for food. He lost 50 pounds in six months, dropping in weight from 190 to 140 pounds. This was partly due to reduced food intake.

Icterus, pruritus, dark-colored urine, and clay-colored stools developed. When the patient was admitted to the hospital the icterus index was in the neighborhood of 45. While the patient was being studied medically, the icterus index rose after a few days' interval to 65, and previous to the time of his operation, which was done around June 10, 1947, it reached 90.

The liver was enlarged down 4 fingerbreadths below the costal margin. It is essential in establishing a diagnosis of cancer of the pancreas that the liver is enlarged in the presence of obstructive jaundice. Whether one feels the gallbladder or not, the liver must be enlarged. Sometimes the gallbladder is pushed so far laterally by enlargement of the liver that it cannot be felt, but usually with care one can feel a rounded mass projecting below the firm, sharp edge of the liver. This is necessary to establish the diagnosis of malignant disease in a patient with obstructive jaundice. It is usually, but not necessarily, painless.

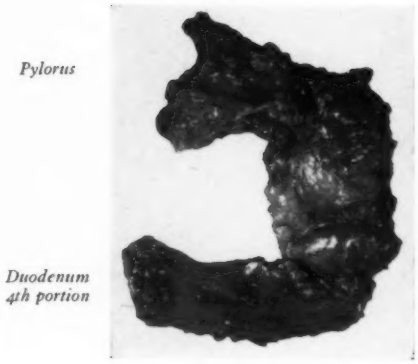


Figure 8. Resected specimen, carcinoma of ampulla, serosal surface. Patient living after five years without symptoms.

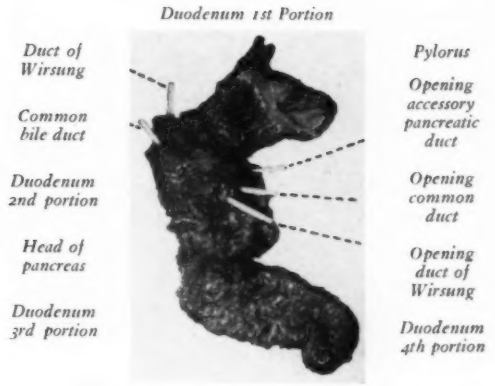


Figure 9. Mucosal surface of specimen in Figure 8, showing submucous invasion of carcinoma of ampulla involving the openings of the accessory pancreatic duct, duct of Wirsung, and common duct.

The condition may be associated with other biliary tract disease, such as stone, in an appreciable number of cases.

This man was operated on and a radical pancreatoduodenectomy was performed.

His immediate postoperative recovery was satisfactory but on his seventh postoperative day a copious amount of clear fluid began to drain from his abdominal wound, indicating a pancreatic fistula. For a period of six weeks this drainage continued as high as 600 cc. of irritating fluid daily.

This man has regained his weight. He has had no recurrence of icterus. The liver has shrunken and he is in excellent condition.

I should like to call attention to some of the important findings in this case for which I am indebted to Dr. Thomas and Dr. Elman.

A deformity of the duodenum was demonstrated. That, in this patient, is important in establishing the diagnosis. This was a carcinoma of the ampulla of Vater invading the duodenal wall. This picture may be produced without obstructive jaundice by duodenal ulcer in the second portion of the duodenum.

A pancreatic fistula developed because the duct of Wirsung was not anastomosed. It is my opinion and experience after having anastomosed the duct of Wirsung 69 times, that most of the complications of resection for carcinoma of the pancreas are related to failure to put the duct of Wirsung into the intestinal tract. Furthermore, few patients will gain weight properly or handle food properly after operation unless this has been the case.

These patients are poor surgical risks, and everything should be done to improve their status before a radical resection is done. It has been necessary in 50 consecutive resections performed in our clinic to do a two-stage operation in two-thirds of the cases (Figure 4). The easiest first stage is cholecystojejunostomy, which will not interfere with the subsequent resection. An antecolic loop of jejunum is brought up and anastomosed to the full width of the gallbladder. Even if you do not choose to do the resection, if you think it is a favorable case you will be doing your best by this patient if this operation is carried out (Figure 4), and give him the chance of possible subsequent resection without too much technical difficulty.

Figure 5 shows the anastomosis to the duct of Wirsung. It is not a difficult procedure. As I have said, we now have done this in 69 cases.

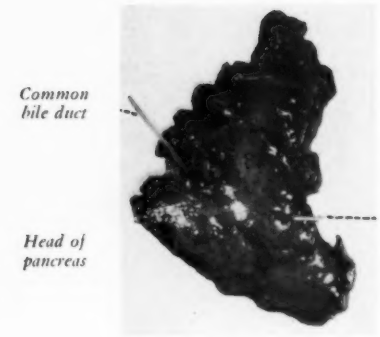


Figure 10. Resected specimen, serosal surface; patient living after four and one-half years.

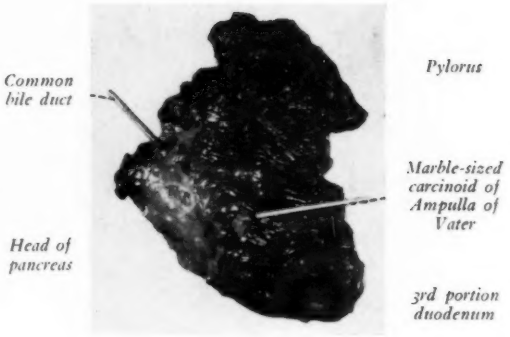


Figure 11. Mucosal surface of specimen in Figure 10, showing ulcerated carcinoid of ampulla of Vater.

You will see in the upper part of the illustration that a tube has been implanted in the duct of Wirsung and an end-to-side anastomosis has been done.

In Figure 6 is shown the completed operative procedure and the technic as worked out by us in our clinic. You will see an antecolic end-to-end gastrojejunostomy, then an entero-enterostomy, then a pancreatojejunostomy, and finally, a choledochojejunostomy or cholecystojejunostomy, depending on whether it is a one-stage or two-stage procedure.

Figure 7 shows the status twelve days after operation. No pancreatic fistula had developed because of the anastomosis of the duct.

I should like to show you the specimens taken from 2 patients. Most of us have the idea that if cancer of the pancreas is present, little can be accomplished. In 50 patients on whom we have operated there have been 9 operative deaths, a mortality rate of 18 per cent. A patient who was operated on five years and two months ago, is at present normal in every respect; she has had no symptoms since her operation over five years ago (Figure 8).

Figure 9 shows an ulcerating tumor of the ampulla in this same patient which had spread to involve the entrance of the common bile duct, the entrance to the duct of Wirsung, and also the accessory pancreatic duct or duct of Santorini. One gland along the border of the duodenum was involved but the patient still remains well.

The next patient is a man of 64 who was operated on (Figure 10) a little over four years ago. He has continued to be well after radical pancreatoduodenal resection. Figure 11 shows this ulcerating tumor with metastases to regional lymph nodes; this proved to be a carcinoid of the ampulla of Vater.

It is our opinion that an operative procedure has been developed through the efforts of many surgeons which not only gives us a reasonable opportunity to eliminate and remove carcinoma of the pancreas with great immediate improvement, with a minimum, perhaps, of complications, but furthermore, over a period of some years the mortality has been gradually reduced. In a group of 50 patients who have had this operation, in our experience, the rate so far during a period of observation of from one to five years has been approximately 40 per cent survival without the appearance of any evidence of recurrence.

DIAGNOSTIC CLINIC

The Diagnosis and Treatment of Hydronephrosis

HERMAN L. KRETSCHMER*

UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE, CHICAGO

THE PATIENT we will discuss here is 58 years of age. She came to the outpatient department at Barnes Hospital on February 21, 1947, and I am indebted to that department for the privilege of presenting her to you.

Two months before she came to the clinic, she noticed a mass in her abdomen. In September 1946, she developed attacks of nausea and vomiting. These attacks occurred every week or two. Following these attacks, she lost weight, tired easily, and had a dull ache in her flank. She also complained of frequency of urination, both day and night, so that she was obliged to void every two hours.

On physical examination the abdomen was rather prominent. A mass about the size of a large grapefruit was felt in the left upper quadrant. This mass was markedly tender, freely movable, and slightly irregular. No stone shadows were seen on roentgenologic examination.

An intravenous urogram showed the presence of a large hydronephrosis on the left side. There was no visualization of the dye on the right side.

*Professor of Urology (Rush), University of Illinois College of Medicine; President of the Interstate Postgraduate Medical Association of North America, 1948.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

Cystoscopic examination revealed the presence of marked trabeculations and some bladder diverticula. The right ureteral orifice could not be found on the first or subsequent cystoscopic examinations. The left ureteral orifice appeared normal.

This patient was operated on and a plastic operation at the ureteropelvic junction was carried out.

DR. KRETSCHMER: Madam, how do you feel?

PATIENT: Fine.

Examination shows the presence of a scar. The most recent intravenous urogram still shows the presence of some hydronephrosis. When this urogram is compared with the film which was made before the operation, a great diminution in the size of the hydronephrosis is evident. This lady has had a wonderful result and I believe there will be still further improvement in her case. She states that she feels very well and is stronger than before her operation.

She mentioned a very interesting symptom; namely, that when she washes on the washboard and bends over it, she has pain in her flank. I believe this is due to the fact that the hydronephrosis does not completely empty. The reflex nausea and vomiting have disappeared. The frequency of urination is still present and is probably caused by the persistence

HERMAN L. KRETSCHMER

of a urinary infection due to Bacillus pyocyaneus.

From the history and physical examination, it was evident that the mass in the left upper quadrant was renal in origin. An intravenous urogram showed the presence of a large hydronephrosis on the left side. Because there was no visualization of the dye on the right side, repeated cystoscopic examinations were made to determine the status of the right kidney. They failed to reveal the presence of a ureter on the right side. This patient has but one kidney and this kidney is the seat of hydronephrotic change. The diagnosis, therefore, was obvious: hydronephrosis in a solitary kidney.

I SHOULD like to dwell on the interesting fact that the cystoscopic examination showed the presence of diverticula. Diverticula, it is now believed, are always congenital in origin and due to obstruction at or in front of the neck of the bladder. They are rarely observed in women; thus, the presence of diverticula should at once cause us to suspect that this patient has an obstruction at the neck of the bladder. Therefore, in addition to management of the hydronephrosis, our attention must be directed to her bladder.

Since her operation, this patient has had an uneventful convalescence. It can be seen by comparing the pyelograms that were made that the hydronephrosis is smaller, the pain is less, and the nausea and vomiting have disappeared. A recent examination showed that the elevated nonprotein nitrogen level has returned to normal (33 mgm. per cent). On the other hand, she still has some urinary infection as evidenced by the pus and bacteria in the urine, and some frequency of urination.

The urinary infection did not improve following treatment with penicillin, sulfadiazine, and sodium acid phosphate. It is evident, therefore, that she has some infection either in her bladder due to obstruction at the bladder neck, or residual infection in her kidney pelvis. If she does not have residual urine, it might be well to catheterize her ureter and obtain urine for bacteriologic studies. In view of the fact that antibiotics have not been of much help, it might be well to dilate her ureter or at least irrigate her kidney pelvis with silver nitrate (2 per cent).

The symptoms of hydronephrosis are not always typical. You are all familiar with the fact that in some patients hydronephrosis may result in complete atrophy of the kidney and there are no symptoms referable to the urinary tract. In a certain group of patients, hydronephrosis is discovered in a more or less routine manner. Many such patients with hydronephrosis consult the internist because of some stomach or intestinal disturbances and routine intravenous pyelograms reveal the cause of gastrointestinal symptoms to be due to hydronephrosis.

Let us now consider the subject of hydronephrosis in its broadest aspects. The most important problem in any case of hydronephrosis is the determination of the underlying pathology. It is to be remembered that the causes

TABLE 1
UROLOGIC CAUSES OF HYDRONEPHROSIS

- KIDNEY
  - CONGENITAL ANOMALIES
    - Form
    - Size
    - Number
    - Position
    - Vascularization
  - LESIONS OF PELVIS
    - Stone
    - Tumor
    - Blood clots (cause?)
  - URETEROPELVIC JUNCTION
    - Stone
    - Stricture
    - Aberrant artery
    - Periureteral adhesions
    - Narrowing at ureteropelvic junction
  - URETER
    - Stone
    - Stricture
    - Tumor
    - Blood clots
    - Periureteral adhesions
    - Compression by tumor
    - Cystic dilatation at vesical end
    - Valves
    - Atony
    - Anomalous insertion
- BLADDER
  - ANOMALIES
    - Ectopia
    - Diverticulum
    - Other anomalies
  - TUMORS
    - Carcinoma in region of ureteral orifice
    - Papilloma in region of ureteral orifice
    - Extensive carcinoma
  - HYPERTROPHY OF INTERNAL URETERAL RIDGE
- URETHROVESICAL
  - LESIONS OF PROSTATE
    - Chronic prostatitis
    - Benign prostatic hypertrophy
    - Carcinoma
    - Bars and contractures
    - Cysts
    - Posterior valves
    - Hypertrophy of verumontanum
- URETHRAL LESIONS
  - STRICTURE
    - Congenital
    - Acquired
  - PHIMOSIS
  - OTHER RARE LESIONS
    - Stone
    - Tumor
    - Diverticulum
    - Urethrocele

TABLE 2
EXTRAURINARY CAUSES OF HYDRONEPHROSIS

- PREGNANCY
- GYNECOLOGIC LESIONS
  - UTERUS
    - Carcinoma
    - Fibroid
    - Endometriosis
  - OVARY
  - INTRALIGAMENT (CYSTS AND TUMORS)
  - VAGINAL CARCINOMA
- GASTROINTESTINAL
  - RECTUM
    - Carcinoma
  - COLON
    - Carcinoma
- RETROPERITONEAL
  - Tumors
- CENTRAL NERVOUS SYSTEM
  - Tabes
  - Myelitis
  - Spinal cord tumors
  - Compression fracture

for hydronephrosis are varied. It is a relatively common urologic condition. As I have mentioned, it may exist as a silent condition and may never produce symptoms referable to it. In some cases, however, the symptoms are atypical, and the most important problem is the determination of the underlying cause. The causes of hydronephrosis may be urologic or extraurinary in origin, as shown in Tables 1 and 2.

From a review of the multiplicity of causes, it is obvious that there is no specific treatment for the hydronephrosis, but that treatment must be directed towards removing the cause. In a case of hydronephrosis, such as the patient I have discussed, it is obvious that she has an obstruction at the ureteropelvic junction. The obstruction generally is due to the presence of a stone, a stricture, an aberrant artery, or periureteral adhesions.

The management of the patient with periureteral adhesions is relatively simple. One divides and removes the bands of adhesions. In some patients it may be necessary to do a nephropexy. In the patient with an aberrant artery, the question of whether the aberrant artery causes the hydronephrosis or whether the hydronephrosis began independently of the aberrant artery arises. When the aberrant artery is small, i.e., when it supplies a small segment of kidney, the artery may be divided. On the other hand, if the artery is large and supplies a large segment of the kidney, it may be necessary to transplant the ureter to avoid obstruction by the aberrant artery.

The patient with a stone at the upper junction calls for a pyelotomy and removal of the stone. The patient with a stricture must be operated on. The number of operations that have been recommended for management of this condition are legion, and I shall not discuss the various advantages claimed for the operations devised by the different authors. Recently Davis of Philadelphia recommended a simple procedure of dividing the stricture and splinting the ureter with a small, soft rubber catheter. It is hoped that this simple procedure will accomplish the desired results, since it is technically much easier and simpler to perform than the various types of plastic operations.

DIAGNOSTIC CLINIC

The Farmer's Back

ROBERT D. SCHROCK*

UNIVERSITY OF NEBRASKA, OMAHA

In our midwestern section of the United States, the problem of "the farmer's back" has been far more disturbing and more frequently encountered during the past ten years than in any previous period in our experience.

"The back in industry" has received many pages of attention in medical literature. Farmers are in the essential industry of food production. As self-employers, they are not influenced by disability covered by compensation insurance. Farmers, as a rule, are eager producers and possess a "will to work" and a "will to get well." These attributes are valuable aids to effective therapy.

The relative increased incidence of back disabilities in farmers is, in our opinion, explainable by the following causes: (1) chronic fatigue due to long hours of work and lack of adequate help; (2) minor trauma, frequent and prolonged, from machinery that is twisting and vibratory in type; (3) decreased muscle strength as a result of motorization of farm equipment; (4) education by the press and medical profession, and (5) improved financial status.

*Professor of Orthopedic Surgery, University of Nebraska, Omaha.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

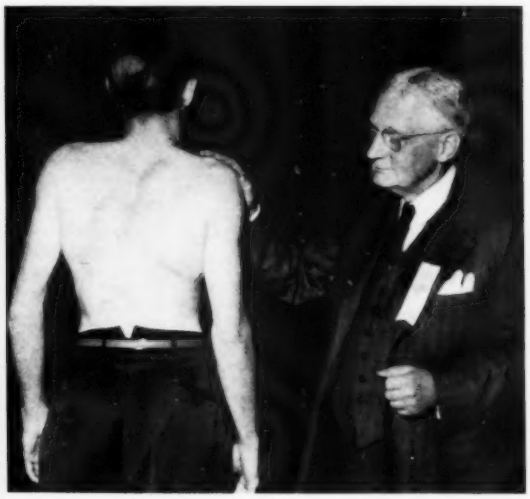
At the Cleveland meeting in 1946, the problem of "low back pain" was presented from the standpoint of examination and diagnosis. This presentation will emphasize more definitely the therapy in the various conditions.

EPIPHYSITIS VERTEBRALIS JUVENILIS

The incidence of this condition in farm boys and girls has decreased. Life on the farm for growing children is less arduous than in the previous decade. The viewpoint of farm parents is less adamant than in days gone by; there has developed a greater respect for the human "growing critter"; thus, greater protection against undue physical strain has resulted. These altered and more intelligent viewpoints are readily traceable to the activities of the 4-H Clubs which so broadly cover this great central farm area. These clubs teach the modern concepts of nutrition and health.

The severe dorsal rounding which was seen not infrequently twenty-five years ago is now, in our experience, a rarity. The family and family doctor have been major factors in effecting the disappearance of this clinical entity. At present, when these youngsters complain of high back pain, they receive early attention before deformity occurs. With adequate nutrition, minor medication, and light external sup-

Figure 1. Epiphysitis dorsalis vertebrae, mild degree.



Dr. Schrock with a patient, showing epiphysitis of vertebrae, in low dorsal region, involving upper lumbar as well, with marked deformity, loss of normal dorsolumbar contour, definite increase in lumbar lordosis.

port, symptoms disappear within six months, and bone growth in the vertebral epiphyses is within normal limits in one year.

During the past ten years an effort has been made to accuse a misbehaving thyroid gland of being contributory to these disorders of growth. Investigations, to date, do not show complete agreement in their conclusions. It is agreed that an adequate milk intake, with consistent use of cod liver oil or its derivatives, is good medicine. Indiscriminate use of thyroid extract in these children and laxity in continuous clinical observation may lead to untoward dangerous effects.

ACUTE TRAUMATIC MYOSITIS

Acute myositis, traumatic in origin, usually results from sudden strain in unanticipated adverse positions, or from injudicious effort during a state of exasperation. The muscle or aponeuritic injury is frequently to the sacrospinalis. Early muscle spasm results as a protective physiologic mechanism. This painful spasm prevents further damaging activity. Normal repair processes, when undisturbed, require two to three weeks. Adjuvants to recovery are rest, local heat of moderate degree, and relaxing massage. The use of "pain killers" and local anesthetics is still a debatable procedure except from the standpoint of quick and temporary relief. There is an increasing tendency toward "trigger point" injections for many acute sprains. The procedure may be desirable under certain conditions but widespread use is, in our opinion, not to be recommended.

ACUTE INFECTIOUS MYOSITIS

The symptomatic diagnosis of "lumbago" is more understandable to the patient than is the etiologic diagnosis of acute infectious myositis. The history may show recurring attacks of "lumbago" with increasing frequency. These attacks are precipitated by undue lifting strain, exposure of an overheated back to quick cooling, or sleeping in a draft, or may result subsequent to a minor sore throat, toothache, blocked sinus, or short period of constipation. These re-

Skeleton brace with Taylor bars.

Skeleton back brace—back.

Skeleton back brace—front.

current attacks of "lumbago" are precursors or prodromals of the chronic fibrositis of middle age, and the osteoarthritis of later years.

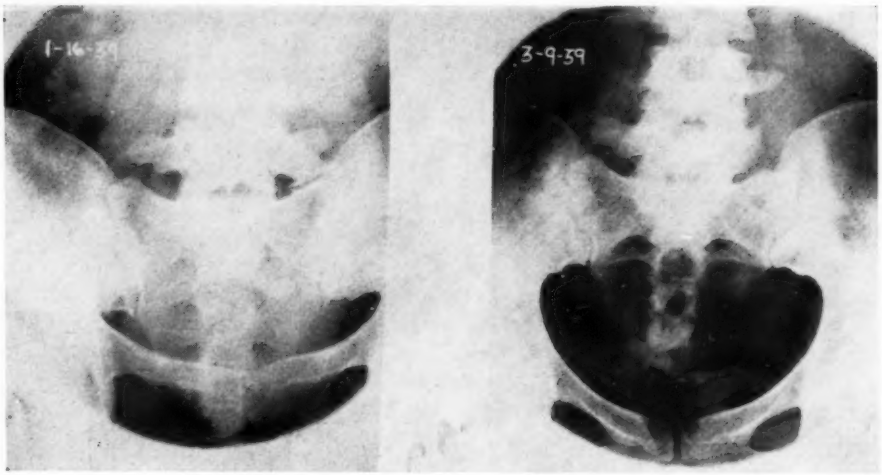
Prophylactic treatment is directed toward meticulous search for foci of infection and judicious removal of the demonstrable foci. Multiple foci may show infections of differing types, but with synergistic effects upon muscle or joint. The major effect may be sufficient to maintain the patient's general health at a low level, and so offer less resistance to the toxic effects of absorption. Warm clothing, with slow cooling after exertion, prevents sudden changes in capillary circulation and materially aids in removal of fatigue products from the heavy musculature of the back. Few middle-aged backs will withstand the rigor of cold showers.

The definitive care is directed toward relief of muscle spasm through local heat of gratifying dosage, massage to stimulate circulation, and salicylates to the saturation point. Active stretching, with motion limited to the pre-pain point, is of value. Overactivity and overstretching will only prolong the attack.

CHRONIC MYOSITIS, MYOFASCIITIS, AND FIBROSITIS

THE clinical "stiff back," presenting some limitation of motion, generalized increased muscle firmness, lack of elasticity, and diffuse tenderness, is given a variety of names. The lack of definitive terminology is evidence of our present concept of the basic condition. There is a comparable lack of uniform agreement as to its etiology, and not too definite an idea of the over-all pathology. The motor mechanism of the back is complicated. Muscles, as a result of repeated trauma, low grade infection, and disuse with resulting poor blood supply, may undergo degenerative changes chiefly showing as fibrous tissue. This leads to structural shortening of muscle, muscle sheaths, and aponeurotic attachments.

Gliding motion in the intermuscular planes is essential for free mobility. Hemorrhage or exudate within the fascial spaces, if not promptly absorbed, becomes organized tissue with localized fibrous adhesions or complete obliteration of the intermuscular gliding mechanism.



Arthritis transverse process LV articulating on S1—Resection.

Arthritis spine—fusion in good position.

The spinal ligaments gradually lose their elastic tissue elements, and the back presents the board-like aspects of an advanced degree of fibrosis of all soft part structures.

Therapy in the advanced case is prolonged, arduous for patient and doctor, and too often discouraging for all concerned. Elimination of the so-called "rheumatoid" elements is essential for ultimate success. Any and all physical therapy measures for promotion of local circulation are valuable. The most valuable agent is active exercise by the patient, guarded stretching, and back mobilizing efforts without overactivity.

The method of determining the most beneficial dose of activity is one of trial and error. It is in this type of back disability, when "trigger point" tenderness is presented, that injection of local anesthetics proves most satisfactory. Manipulation of the fibrositic back, under general anesthesia, is not as yet an established procedure. A supporting apparatus, intermittently used, will permit these patients to be partially productive.

OSTEOARTHRITIS OF SPINE

This condition prevails in the age group of "50 years and more." The onset is insidious, may be even symptom-free, or follow the pattern of an infectious myositis. The productive process may be well advanced before it is even recognized.

For complete information of the causes and treatment of arthritis of all types, one needs only to scrutinize an editorial in the J.A.M.A., October 3, 1947. The frank confession of failure is commendable. The honest recognition of certain useless therapeutic methods is highly laudable. The editorial pulls no punches, and demonstrates a high degree of courage.

The usual reason for pain in osteoarthritis of the spine is trauma superimposed on an already established and irreversible pathologic change. Recovery from the trauma is prolonged and hence, help is sought. Our help is limited to careful analysis of activities that produce trouble, and to urging their avoidance. Adaptation of the back to its capacity is essential. Maintenance of the general health of the patient at a high level, and the use of a supporting back brace are helpful.

SPONDYLOLYSIS—SPONDYLOLISTHESIS

In this category, patients present a lumbar vertebra, practically always the fifth, in which the laminae of the neural arch are connected to the posterolateral aspects of the vertebral body with fibrous tissue rather than with bone. This defect adds to the architectural weakness, and diminishes resistance to mechanical strain. Due to the anterior inclination of the sacrum and the normal anterior lumbar curve, there is at the lumbosacral junction a shearing force that tends to thrust the fifth lumbar forward on the sacrum. This gliding forward action is gradual, and may take place in varying degrees without symptoms of real pain. These patients, under conditions normal to them, have "backaches" made worse by overuse or repeated heavy lifting. Severe twisting or lifting strains may produce minor backache but sudden forward shifts are accompanied by severe pain and persisting low back disability. Frequently there will be associated nerve root pressure or stretch, giving rise to lateralized or radiating pain over the distribution of the fifth lumbar or first sacral nerve, unilaterally or bilaterally.

The literature on this condition is extensive. There is still no uniformity of opinion in classifying this condition as a congenital anomaly, or as a trauma at birth, produced by certain maneuvers in making the newborn breathe. Rarely is the condition diagnosed early in life, for displacement, if present, is minimal. It proceeds gradually and slowly. Some adolescents may complain and refrain from exposing their backs to the strains normal for such ages. Many adults recognize their possession of a "weak back" and yet continue with heavy work until pain becomes disabling. This occurs most frequently after the age of 35, when muscle tone, strength, durability, and quick recovery from fatigue tend to decrease.

In this middle and older age group, acute

trauma and chronic overfatigue produce disability greater than anticipated and recovery from a "sore back" does not take place.

When spondylolysis is discovered in childhood or adolescence, conservative care (sufficiently informative) and prophylactic observation may be adequate. In late adolescence and in adult life, external bracing is essential until internal bracing can be accomplished by means of a low back fusion.

There is a general consensus, supported by many clinical observations, that forward displacement of the fifth lumbar takes place gradually; that correction of the displacement is impossible in grades 3 or 4 and improbable in grades 1 and 2; that operative fusion is most desirable and more successful when displacement is minimal.

Spondylolisthesis, Grade III.

CONGENITAL MALFORMATIONS

Detailed studies of patients with low back pain reveal a high incidence of architectural abnormalities in the spine. Osseous variations

Spondylolisthesis, Grade I—Low back fusion.

Spondylolisthesis, Grade I.

are most frequent in the lumbrosacral region, which is admittedly the recipient of most back strain. Back strength is determined by its weakest region. Abnormal architecture indicates structural weakness which many times lacks adequate muscle strength to compensate for bone defects. Low back decompensation is more frequent in the presence of congenital malformations of the lumbosacral region.

This statement does not mean that all backs showing congenital malformations cause trouble for their possessors. Fortunately, many backs do not have to withstand the wear and tear of farm life.

When low back decompensation does occur, it is sometimes possible for the farmer to plan his work in such a way that he can avoid those recognized strains. The intelligent farmer will use his head and the other fellow's back. Back efficiency and symptomatic relief is obtained with a light nonrigid low back support, to be used as the occasion demands. Conservative care is indicated until proved a failure. The trial period is usually three to six months. When conservative measures fail, low back fusion is indicated.

LOW BACK INJURY WITH PAIN IN THE LOWER EXTREMITIES

During the past ten years, the problem of herniation of the nucleus pulposus, with associated compression neuritis, has properly received major attention. The enthusiasts who early proclaimed this lesion as the causative factor in all low back pain with sciatica, have gradually had their enthusiasm tempered by more adequate follow-up studies of their generous and brilliant laminectomies. The early use of contrast opaque media injected into the spinal canal is not employed as freely, as closer clinical study is finding methods for more adequate localization of the lesion.

Laminectomies are becoming less generous, and technic has improved. More adequate follow-up studies are demonstrating that resection of the herniated nucleus pulposus in many cases does not give adequate satisfaction to the patient or doctor. There is developing a strong sentiment that low back fusion should be done with all laminectomies. This viewpoint is too radical. However, a combination of congenital malformation and signs of localized nerve root pressure is now being more generally accepted as an indication for low back fusion.

Hemi-vertebra, Lumbar V.

Hemi-vertebra, Lumbar V—Low back fusion.

DIAGNOSTIC CLINIC

Differential Diagnosis, Benign Prostatic Hypertrophy, and Neurogenic Bladders

DALTON K. ROSE*

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

PROSTATIC hypertrophy (requiring surgery) occurs in probably 35 per cent of men past the age of 60. Presented in another way, it occurs in about 67 per cent of all men, with about half of all these cases eventually coming to surgery.

A point of interest is that the term hypertrophy of the prostate makes us feel that the gland has to be large to obstruct the bladder. However, obstructing factors, scar tissue, or a small adenoma which may be buttressed against scar tissue down in the prostatic urethra, will obstruct equally. In other words, you can have a giant prostate with no obstruction and you can have a 2 gm. prostate with considerable obstruction associated with contracture at the vesical neck.

The contracture type occurs in younger men and is associated with infection in all instances. In that respect it is going to be interesting to see what sulfonamides and the new antibiotics do in the next generation to scar type obstruction, whose frequency of occurrence should be reduced.

The adenomatous type is due to senescence, of course, and goes hand in hand with graying hair, bald head, wrinkled skin, etc. Although all men have some scar or hypertrophic changes, only a small percentage of them come to surgery.

The trick of prostatic obstruction is, in my opinion, how rapidly it develops. If one is required to lift an impossible load but is given time enough to develop the necessary strength to lift the load, it may become possible. Although the bladder is smooth muscle, if it is given time when obstructed, it will develop a thick muscle wall back of the obstruction. The obstruction may stop anywhere in life and one may develop sufficient compensation or thickening of the bladder wall to overcome the degree of obstruction. Such a man will notice in particular that he urinates in the morning with a slow stream, due to overfilling of the bladder during sleep and a slight overstretching of the bladder wall, which though compensated now when overstretched, does not force the stream out as easily as it does later in the day when the bladder is emptied more frequently.

Stimulation to the bladder is nothing more nor less than stretch. The stretch reflex, of course, is in smooth muscle just as in striated muscle. The "knee jerk" is stretch reflex. A bladder filled and emptied is in effect a stretch re-

*Professor of Clinical Genitourinary Surgery, Washington University School of Medicine, St. Louis.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

flex. On rising in the morning, a few drops dribble out, then a little more and a little more, and finally a stream when the bladder wall is contracted to a sufficient point that it has strength to overcome the obstruction.

Nycturia is explained in this way: When a man goes to sleep, inhibition by the brain is relatively lost and the thickening bladder wall goes into uncontrolled contraction. This contraction wakes him with a desire to void. He may get up and void or he may roll around in bed in discomfort, but when he finally does get up, he may find that he does not have to void as badly as he did when he was in bed; he is awake, his inhibition is back, and his bladder wall has gone out of contraction. On the other hand, when he carries a residual urine, he may have less nycturia due to a developing pressure anesthesia to his bladder. This occurs in the same manner as when you sit on your hand or lie on your arm. It is a pressure numbness that comes to the bladder when there is either a very high intracystic pressure or a residue of urine in the bladder all the time.

Frequently when a patient comes to you with 1000 cc. of residual urine he has no distressing desire to void. You can remove the 1000 cc. and you will not be able to get back more than 500 or 600 cc. In that split second, so to speak, the pressure anesthesia has partially disappeared even in a bladder wall which became overstrong for a long period before it finally gave way.

DALTON K. ROSE

All of this brings us to the point that prostatic obstruction is not alone the prostatic obstruction; it is in a large part decompensation of the bladder wall. You can prove this just by realizing that if you could always raise intracystic pressure you would never have complete obstruction, although it might come to the point where the stream would be 10 feet long and as large as a darning needle.

To go into an analysis of neurogenic bladder—a misnomer, in my opinion, as the term suggests that the nerves of the bladder are primarily at fault—I do not think it is the bladder itself that is neurogenic, but rather I think the primary nerve damage is to the so-called voluntary sphincter. We have detrusor action but there is no detrusor muscle unless one wants to consider it as the bladder wall. We have already covered the fact that normally the bladder wall changes according to the load that is offered it; if it becomes thick, and if the block is such that the back pressure continues indefinitely, it becomes overstretched and has no expulsive power. There are many gradations between, which you can readily realize, and all these gradations give characteristic symptoms of either frequency in the early day, with a thickening bladder wall, or, paradoxically, incontinence at the time when it overflows, when the bladder is stretched thin and always full but always running over.

I have reported previously a standard for normal bladder function. I do not believe these standards can be proved until we have satisfactory x-ray motion pictures. However, these

ideas of bladder physiology stand the scrutiny of all investigative work up to this time and also the scrutiny for analysis of all types of bladder symptoms. The main idea is that the bladder is a voluntary-involuntary organ. It is not at all unlike swallowing. You chew voluntarily to a certain degree, swallow, the food goes down to the involuntary portion of the swallowing apparatus, where it gets away from you and away it goes; you cannot recall it. The first part is voluntary and the last part is involuntary, and so it is with urination. If the bladder were not locked, so to speak, by voluntary control, there would be no time or place for emptying the bladder; it would run all the time or spasmodically.

What is the voluntary action? It is the anterior perineal muscles. You can see a great deal of this action in cystoceles, rectoceles, and urethroceles. It is the perineal muscles anterior to the anus, although the entire pelvic sling has something to do with it. These muscles are, of course, striated, voluntary, and innervated by the pudic nerve, which is of sacral origin and is thus related to the sciatic nerve, which is lumbosacral in origin. But that is not of great importance except in physiologically differentiating certain types of neurogenic bladders, in which the anal sphincter, voluntary bladder sphincter, and the legs exhibit similar nerve changes from spastic to atonic. I wish to differentiate uncomplicated types of neurogenic bladders that you can diagnose by feeling the anal sphincter only, without any other method.

If the perineum is the voluntary control of a voluntary-involuntary sphincter complex, what are the steps in urinating? The first step is to choose the time and place. The next is to lower the anterior perineum, which brings down the internal orifice of the bladder. A thin muscle called the trigonal muscle bridges the internal orifice of the bladder; when the perineum pulls down the internal orifice of the bladder, this muscle, going through and over the floor of the internal bladder orifice, is lowered, contracts, and so lowers and broadens the internal orifice. Herewith ends the voluntary phase of urination. Urine now runs over into the posterior urethra to stimulate involuntary bladder contraction. Control, therefore, can voluntarily be exerted by pulling up on the perineum. You have seen children run crosslegged. Why do they do this to keep from urinating? They are using their adductor muscles to hold up the anterior perineum, because they feel the threat of urine entering the posterior urethra and they instinctively know if that happens that the bladder will go into involuntary contraction and they will wet their pants. This function in analysis holds out very well in all types of incontinence, in many kinds of neurogenic bladders, and in cystoceles, urethroceles, and rectoceles. When there is constant leakage into the posterior urethra, the expulsive force becomes more violent, and therefore all factors toward emptying the bladder involuntarily are exaggerated, because the bladder is contracted, constantly.

WHENEVER there is urgency of urination, it means that the patient is given time to realize that he is going to lose urine if he cannot get to the toilet in a matter of seconds or minutes. When there is no urgency of urination, it means that urethral sensation is so numbed either by constant water in the posterior urethra (pressure anesthesia) or by pudic nerve change that he is not warned of urine leaking into the posterior urethra. Urgency is a symptom that without doubt decides against incontinence of the bladder, neurogenic of the atonic type.

Neurogenic bladders can vary as time goes on. Let us divide neurogenic bladders into the two general types: the spastic neurogenic bladder and the atonic neurogenic bladder. The spastic neurogenic bladder is one in which the anterior perineum is spastic, and you may expect to have hyperactive knee jerks and possibly some degree of spastic paraplegia. The atonic bladder is typically the tabetic bladder. It is one in which there is demyelinization within the posterior columns; that is, the sensory side of the reflex arc is broken. What does that do? Urine is not recognized within the posterior urethra, because this sensory recognition

is carried through fibers that are carried within the posterior column of the spinal cord.

Let us say that a person has a syphilitic change in his spinal cord; he has tabes dorsalis; he does not know where his foot is; he loses sense of position in space; he is ataxic. His perineum is ataxic and anesthetized also, so he has no reflex tone to his bladder wall. The loss of tone is of the perineum—his anal and bladder voluntary sphincters are atonic. The loss of bladder tone is secondary. When sensation to the posterior urethra is damaged by demyelinization within the posterior columns and urine is not recognized in the posterior urethra, there will be such a weakened reflex to the bladder wall that a residual urine will develop. Urine left behind in the bladder further breaks down the musculature by further pressure anesthesia and a vicious circle is thereby established.

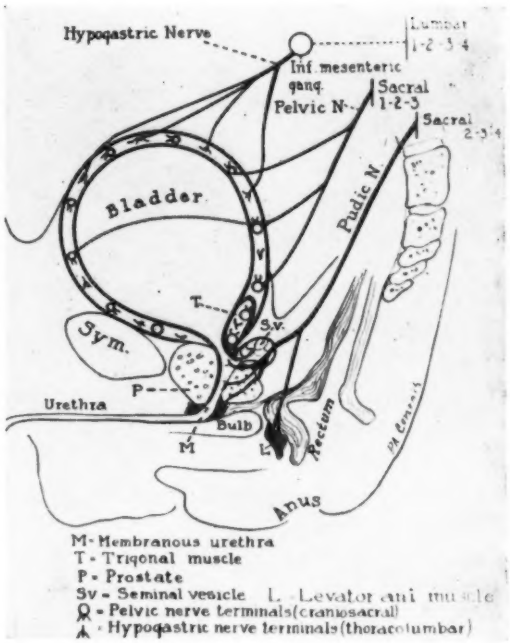


Figure 1. Diagram of the bladder wall with its trigone.

LET US consider one of the most interesting complex types of neurogenic bladders. If one is riding in a closed car and has a collision, he is thrown from his seat and becomes something like a pea in a pod; he is rattled about. He may receive a severe blow on the head which would make him flaccid; his legs would be flaccid, as would his arms, neck, back muscles, etc. If he is now brought to the hospital, unconscious, drooping, he has at that moment, in effect, a tabetic bladder. He has diminished perineal tone.

If one is hit on the head with a hammer and the blow is not lethal, he will have flaccid muscles. However, if the damage to his cerebrum is not great, he will recover, but if at the time of the accident he also received an injury to his spinal cord, such as a hemorrhage or other form of irritation, he may recover with a residual spastic bladder. This will not be all; he will have spastic legs, and a spastic perineum. The spastic perineum means that he can no longer lower the internal bladder orifice voluntarily to start urination by letting water flow into the posterior urethra and so reflexly contract the bladder. He will develop a residual urine back of a spastic perineum, with a spastic anal sphincter.

If this young man (most such cases are boys) is catheterized when the bladder fills up, that catheterization gives him, in my opinion, about a 90 per cent mortality rate—just that one catheterization. How? It depends on whether the spastic changes in his legs and his voluntary sphincter, that is, his perineum, are permanent or not. If it is temporary, he will be all right, but if the damage to his spinal cord is such that he will remain a spastic paraplegic, he will have a permanent spastic bladder (and anal) sphincter and he will never be able completely to empty his bladder again. By catheterizing him we are going to infect him, we are going to contract the bladder wall; an infected contracted bladder kills the kidney function in one of four ways: (1) infection by lymphatic spread, (2) spread through the blood stream, (3) spread up the ureters, or (4) by back pressure, causing infected, dilated ureters

Figure 2. Normal bladder wall.

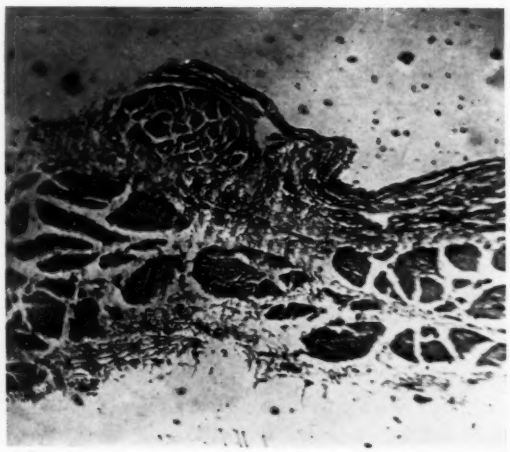


Figure 3. A compensated bladder wall showing the effect of overwork, frequent urination, and/or difficulty in forcing urine through a partially blocked outlet.

and kidney pelves. His one hope is to develop an automatic bladder.

What could you do with him except catheterization? Nothing! Let him overdistend? Then will you kill his kidney function? Not necessarily. If he is overdistended possibly he will get an infection anyway by way of the blood stream. That is true, and if he does it is bad luck, but not poor medicine and "sufficient unto the day is the evil thereof." What would you do with him? Leave him alone and watch his breath for urinous odor, watch his NPN, and watch his general condition. Possibly cystostomy or transurethral surgery will be indicated in such a case.

In preoperative diagnosis of prostatic obstruction, we have almost given up cystoscopy. We have to employ this method occasionally, as any urologist knows. However, intravenous pyelography with a 2-hour "delayed" film will usually reveal the necessary facts, tumor stone diverticulum, and in addition will show the status of the upper urinary tract.

One of the symptoms of any urethral obstruction is a desire to void after emptying the bladder. The patient empties the bladder, but he will tell you, "I don't want to leave the toilet. As soon as I empty the bladder, I feel that I have to empty it again." You might be surprised to find he has only an ounce of residual urine in the bladder.

This is important in that many things can be done to handle these early obstructions besides surgery, and I feel that uncalled for transurethral or poorly chosen (I prefer that term) transurethral on a physiologic basis in the early obstruction is not beneficial. I believe that about 30 per cent of all men past the age of 60 have some urinary trouble—slow stream, slow start, up at night—but they have no intention of undergoing surgery. Two ounces of residual urine is not sufficient to indicate transurethral surgery when the man is not in distress, because such surgery may leave him with an irregular urethra which may mean a permanent urethritis, which sometimes is the cause of frequency and discomfort.

Figure 1 diagrammatically shows the bladder wall with its trigone. The involuntary innervation is unimportant to us clinically. However, the pudic nerve innervating all voluntary muscles associated with micturition is, in

Figure 4. Cystogram showing a round, prostate filling defect in a case of benign, nodular prostatic hypertrophy.

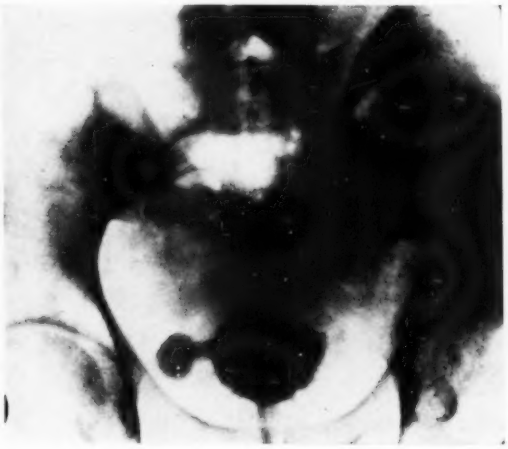


Figure 5. Cystogram of compensated bladder wall, showing the small, benign, scar tissue type of prostatic obstruction of slow development.

my opinion, most important in diagnosing neurogenic bladders. The pudic nerve innervates the perineal muscles, levator ani group, and the weak compressor muscles within the urogenital trigone, as well as other perineal muscles.

Given a markedly atonic perineum in tabes dorsalis, for instance, the perineal muscles are atonic and allow the internal orifice of the bladder to drop from its normal and tonic upward placement, thus lowering the internal bladder orifice which tends to produce incontinence of urine. Furthermore, such a patient will void a weak stream as the bladder tone is diminished proportionately to the loss of sensation in the posterior urethra. The reason for this is that micturition is a voluntary-involuntary reflex. A person first voluntarily lowers the perineum, and *with it the internal bladder orifice,* so that urine may flow into the posterior urethra, reflexly to stimulate the bladder wall to involuntary contraction. In such a case the *voluntary anal sphincter* is correspondingly relaxed; its tone, as determined by digital palpation, is of diagnostic value in certain cases of tabes dorsalis with dysuria, and in all atonic neurogenic bladders.

On the other hand, in cases of spastic paraplegia in which the legs, perineum, and *anal sphincter are spastic,* the spastic perineum elevates the internal orifice of the bladder, facing it upward and forward in a "urine retaining" position. This patient cannot voluntarily institute voiding. He cannot release the spastic perineum, and therefore lower the internal orifice of the bladder so that urine may flow into the posterior urethra reflexly and involuntarily to stimulate contraction of the bladder wall. The spastic anal sphincter is also of diagnostic value here. However, such an anal sphincter at first palpation may be spastic and then *actively* open to simulate an atonic sphincter. Also a relaxed anal sphincter in certain neurogenic bladders first may be relatively atonic to be stimulated into spasticity by a palpating finger. These movements by the perineal muscles influence the position of the internal bladder orifice, clinically reflected by

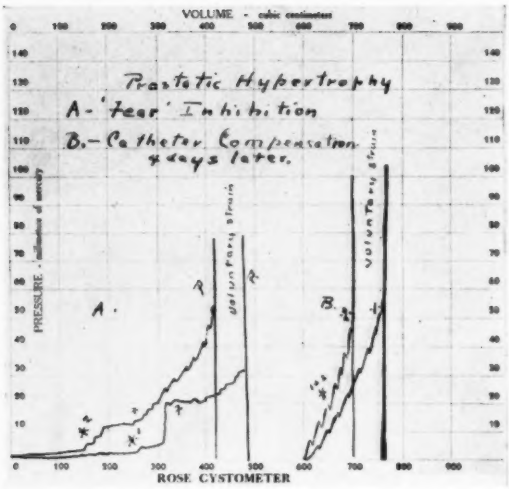


Figure 6. A cystometrogam graph which correlates intracystic pressure and bladder capacity.

symptoms of atypical retention or incontinence of urine, also the perineal muscles determine the state of the anal sphincter.

A normal bladder wall is shown in Figure 2. Back of the interdependent, voluntary-involuntary sphincter operates a smooth muscle reservoir, the bladder. Its musculature varies in thickness, with the degree of distention existing at the time that a section of its wall is made. We have in this figure a normal wall—note three layers of smooth muscle and the size of the smooth muscle bundles.

A compensated bladder wall (Figure 3) shows the effect of overwork, frequent urination, and/or a difficulty in forcing urine through a partially blocked outlet. Contraction will give thickness of wall but not such an increase in size of the muscle bundles. The time element is important in these changes. A rapidly developing bladder obstruction will not give time for bladder wall compensation as does an obstruction of slow development. Compare this bladder wall section with Figure 2, particularly the size of separate muscle bundles.

Figure 4 is a cystogram showing a round, prostate filling defect. In this instance of benign, nodular prostatic hypertrophy, a gland of 150 gm. was removed by one-stage suprapubic prostatectomy. The bladder was not coarsely trabeculated; therefore the obstructive factors developed recently. Analysis of symptoms verified this fact. The large bladder capacity also strongly suggests recent obstruction as a thickening or compensating bladder tends to smaller capacity.

A CYSTOGRAM may serve instead of cystoscopy although the latter is more accurate; it may be chosen in instances where you wish to omit cystoscopy in cases of poor risk, hemorrhage, or a large median lobe. *If the opaque media is of the same density as the intracystic lobe of the prostate, no filling defect will be seen.*

A cystogram of compensated bladder wall is shown in Figure 5. In contrast to Figure 4, this presents the small, benign, scar tissue type of prostatic obstruction of slow development. This type, beginning early in life as a rule, gives the bladder wall time to thicken and in this instance to herniate a diverticulum through a congenital hiatus or weak spot in the bladder wall. The "neck" of the diverticulum "measures" the thickness of the bladder. We should expect to do transurethral surgery in such a case. The bladder, when relieved of its obstruction, will return to normal thickness, and I believe the small diverticulum, after operation has lessened intracystic voiding pressure, will resolve, in this instance, into a shallow cellule.

Figure 6 is a cystometrogram graph which correlates intracystic pressure and bladder capacity, and gives opportunity to place degrees of bladder filling sensations on the pressure-capacity graph.

A retention catheter, depending upon the type of bladder wall, contracts the wall either weakly or strongly, and correspondingly may abrase its mucus membrane. Also its presence in the posterior urethra offers a stimulation to contract the bladder reflexly, as urine in the posterior urethra normally effects this reaction. These reactions in a compensated bladder often

Figure 7. Cystogram of a decompensated (atonic) bladder. Note sag of internal orifice area.

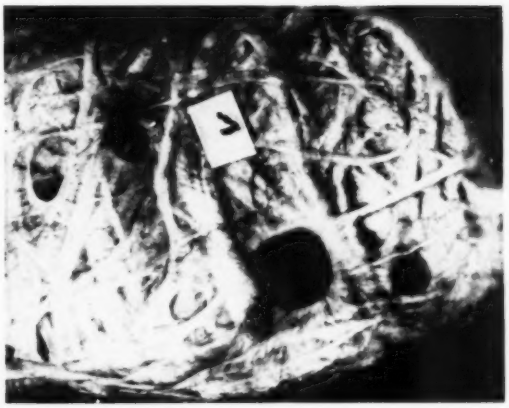


Figure 8. Photograph of a section of interior of a bladder decompensated by back pressure.

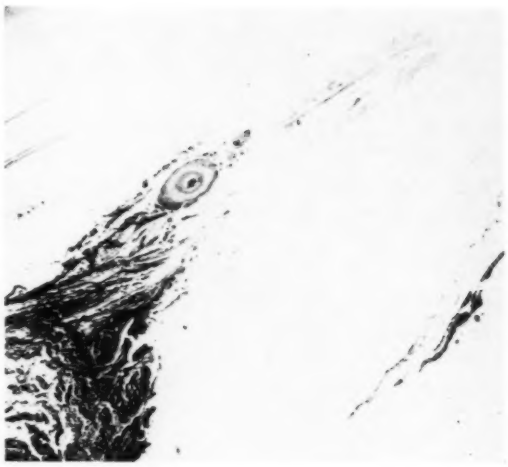


Figure 9. Cross section of a large thin-walled diverticulum.

result in hemorrhage, diffusion of infection, and poor drainage, the latter due to block by blood clots or edematous bladder mucosa.

This cystometrogram was made by *two usual* fillings. The asterisk 1 and 2 mark the "first desire to void," point "F" 1 and 2 the "sense of filling," and "P" 1 and 2 "pain of overdistention" in first and second curve. The first filling stimulates the bladder by stretch reflex, that is filling and emptying so that curve 2 is shorter (less capacity) than curve 1.

Through cystometric work I feel that the principle of "bladder decompression," i.e., catheter drainage before cystostomy, as applied in a poorly explained effort to protect kidney function, is not only incorrect physiology, but actually increases mortality rate in suprapubic prostatectomy.

Figure 7 is a cystogram of a decompensated (atonic) bladder wall with some regurgitation up the right ureter. Note sag of internal orifice area. Weakness is most marked at the dome and left lateral wall, but even with this the thicker portions, notably the right floor, show fairly coarse trabeculation, suggesting early long resistance to back pressure, residual urine, development period, before its musculature decompensated. A tabetic type bladder would not thicken (compensate) before decompensation—it would lose strength as soon as nerve damage became progressive, and therefore would not show coarse trabeculation. This bladder has

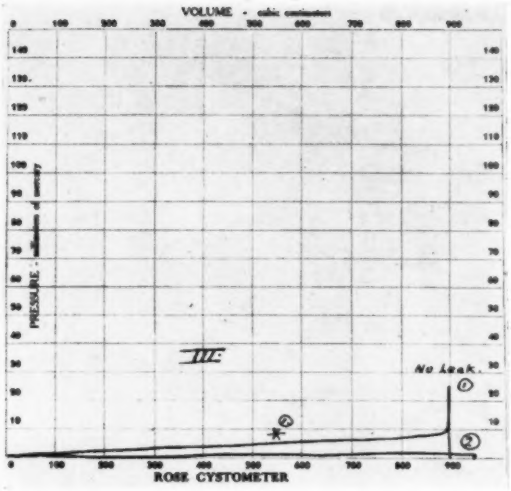


Figure 10. Cystometrogram in tabes dorsalis with large infected residual urine.

great recuperative powers, though probably not 100 per cent.

A section of the interior of a bladder, decompensated by back pressure is illustrated in Figure 8. Long years of overwork, both frequency of urination during the years when the thickening and possibly early infected bladder wall were able to overcome the prostatic obstruction, and an *increased intracystic pressure,* necessary to force urine through a partly blocked internal orifice and the prostatic urethra, produced the coarse trabeculations, diverticula, and eventual decompensation. This bladder wall, thickened, herniated by diverticula and cellules, and even if infiltrated by scar tissue, can return to near normal function, providing the diverticula are not too large and thin-walled, in which case they will absorb a lot of the voiding intracystic pressure and a large residual urine will remain even after prostatectomy. A cystometrogram of this bladder would show large capacity, a reduced intracystic pressure, and normal sensations. The anal sphincter would be normal.

Figure 9 shows a cross section of a large thin-walled diverticulum. It requires little imagination to visualize how such a weakened area in a bladder would absorb the voiding pressure to leave a large residual urine in the bladder, as well as in the diverticulum.

A cystometrogram in tabes dorsalis with a large infected residual urine is pictured in Figure 10. This cystometrogam shows markedly diminished sensation and poor reflex innervation from the urethra to the bladder wall. The bladder musculature actually overstretches by the first filling—note that filling II is lower than filling I. The anal sphincter would be markedly relaxed. Treatment is directed toward reducing the residual urine by transurethral resection of the prostate if there is a hypertrophy or scar thickening about the prostatic urethra by manual expression of urine, by catheterization.

As a rule, catheterization of a neurogenic bladder of the spastic type is dangerous but of this low pressure, or atonic type, it is not only safe but good treatment.

DIAGNOSTIC CLINIC

The Results of Electric Shock Therapy

LELAND B. ALFORD*

ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS

In electric shock therapy we have a method of treating the psychoneurotic states that is shorter, more thorough, and longer lasting than any other approach. The method is truly a milestone in medical progress.

I initially employed insulin for shock therapy, then metrazol, and finally electric shock. I treat a large proportion of my cases by this method, but only when I suspect that other methods might be prolonged and doubtfully effective. The cases are those of referred practice and are neither the worst forms nor the mildest. They are mostly acute or recurrent; few are of long standing.

The patients are predominantly working people who are interested in saving money and resuming their occupations. I believe that electric shock therapy is an immense contribution in both respects.

The danger of fractures and dislocations is almost completely eliminated by giving the patient two nembutal capsules an hour before treatment. The sedative action cushions the shock and complications are rare. I have had no fractures or dislocations in my experience with this method. Occasionally the patient complains of a sore back, but it gradually disappears. I consider the dangers to be similar to those of having a tooth extracted. Advanced cardiac or coronary disease is a contraindication, but milder stages are not necessarily so.

I divide my treatments into courses, and this is a unique feature of our procedure. After a certain number of treatments the memory becomes confused, and I believe that this fact is a measure of their effectiveness. A course is the number of treatments necessary to cause this confusion. In older persons the number may be only four, while in young persons it may be as many as eight. After one course it is necessary to stop and wait about a week and to observe the patient's condition. As treatments are given daily, a course takes approximately a week.

This policy affords a certain standardization, since much time and money are frequently wasted in cases where it cannot be determined whether further treatments are indicated. Two courses are advisable and usually necessary. If there is no lasting result after three courses, the advisability of continuing with electric shock therapy is doubtful in most cases.

In the effort to minimize the expense of ther-

*Associate Professor of Neurology and Psychiatry, St. Louis University School of Medicine, St. Louis.

Presented before the meeting of the Interstate Postgraduate Medical Association of North America, St. Louis, Missouri, October 14 to 17, 1947.

LELAND B. ALFORD

apy, more and more treatments are given as out-patient procedures. The patients come to the hospitals, where beds are supplied for this specific purpose, for a couple of hours and, after the treatment, return home. In hospitalization insurance these treatments count as a day in the hospital, so no expense is incurred by the patient.

The second course, or even part or all of the first course, may consist of out-patient treatments. Occasionally patients continue to work during these treatments.

Patients over 55 years of age are likely to have recurrences within a year or even within a few months, this likelihood becoming greater as the years advance further. Little can be promised to the senile psychotic in the way of lasting results. But there is another procedure which may benefit these patients.

For some patients a regular treatment once every two weeks or every month may keep the condition in abeyance. We have employed this method with some success and I particularly wish to emphasize it here as perhaps being to some extent unique. I do not wish to claim originality for all these different procedures because my colleagues often suggest them to me and I wish to give them credit. Dr. Deppe especially has suggested several very useful approaches, and the matter of giving nembutal to avoid fractures was suggested to me by a nurse following several disappointments with electric shock therapy.

This staggered treatment is also effective in certain paranoid and guilt complex cases, examples of which will be given, which continually recur after courses of treatments. It has enabled some patients to continue work for two years without relapses.

THIS, then, is the general procedure for all types of psychoses. I believe that the best results are obtained with the involutional types and the poorest with manic cases. The involutional case seems to constitute an exception to the rule that the long-standing case is unfavorable. There are instances of cases of five or even ten years' duration being relieved within the course of a few weeks and remaining well. The hyperactive manic type of case seems to relapse quickly, more often than other types, but these are only general tendencies.

It should be explained that nearly all cases improve while treatment is in progress. The unfavorable cases relapse in from one to three weeks after treatment is discontinued. If a relapse does not occur within three weeks, the effect will likely be lasting.

Recurrences in years following electric shock therapy occur as with any method of treatment. It is my impression, however, that such recurrences are less frequent with electric shock therapy than with other methods.

The neuroses are as amenable to electric shock therapy as are the psychoses. It would be a mistake to assume, however, that because they are milder, fewer treatments will be necessary. The neuroses will require as many treatments, on the average, as the psychoses

and there will be as large a proportion of failures, probably larger, because cooperation is harder to obtain. The neurotic patient seeks an easier way out. The acute phases, the acute anxiety and depression states, are the most promising types. Some schizoid neurotics will also respond with a relatively large number of treatments, but the old hypochondriac, the patient who has had aches and pains all his life, should be left alone.

In the neuroses especially much depends on the cooperation and the attitude of the patient. When he genuinely desires relief and shows that he will cooperate, electric shock therapy may be employed in many instances in which it would otherwise not be undertaken. The attitude of the family is also important. Very often an intelligent and cooperative member of the family will determine the success of the procedure.

I believe there are many such cases of neuroses which will never yield to any other type of therapy and therefore electric shock should be kept in mind as an expedient if it can be applied successfully.

I would say in 4 out of 5 cases, or at least 3 out of 4, of psychoneurotic illness, electric shock therapy is a boon. It relieves many who otherwise would get little if any relief. The relief is more thorough and longer lasting; the length of treatment is greatly reduced, often from months to weeks or even days, and the cost and loss of time are likewise lessened.

There still remains the case that responds and quickly relapses. I am unable to predict these cases. One can speak only of percentages. Continually, cases which seem favorable turn out not to be so, and conversely cases that appear unfavorable respond favorably. Even after having given from 1,500 to 2,000 treatments a year since this therapy was first employed, I still cannot predict whether a patient will respond or not. It is not possible to divide the cases into types and to predict by types what the result will be.

This does not apply, however, to the frank chronics, the cases with hallucinations or the long-standing cases where the prognosis is poor and treatments are given only with some definite purpose in view such as quieting the patient. Some patients require treatment either in a sanitarium or by a systematic approach; their conditions cannot be corrected quickly.

How can electric shock therapy be made to reach these resistant cases? I do not know. I have tried increasing the number of treatments; occasionally this system gives good results. I have tried giving treatments beyond the confusion stage, but it is difficult to continue treatments when the patient becomes almost blank. Perhaps such expedients should be investigated further. One such expedient I will mention again later.

Frontal lobotomy for the unfavorable case is, of course, one recourse, and I have tried it in about 40 cases. Fifty per cent or more of these have had fairly favorable results, some of them brilliant.

If electric shock therapy proves ineffective, will the patient be worse off than before? I do not think so. He may be somewhat more active and resistant, but any difference is basically not important. I do not believe there are any permanent harmful results.

There are one or two incidental uses of electric shock therapy. A rather surprising one is in the treatment of general paralysis due to syphilis of the central nervous system. The violent paretic will be subdued by electric shock therapy and rationality will often be restored. I have given paretics electric shock therapy in the hospital until they were restored mentally, and then carried out a course of malaria in the home. My experience with such cases has not been extensive, however.

Another use of electric shock therapy is that following frontal lobotomy where there is incomplete recovery or recurrence of symptoms. Electric shock therapy apparently is more effective after the operation. However, more frontal lobotomy cases have had the benefit of shock therapy before the operation.

The method of staggering treatments has another effect. When symptoms continually re-

cur after courses, I have resorted to the method of having the patient go home, giving treatments at regular intervals, and continuing this indefinitely. Some of these patients continue with their work, with the understanding that they will come in once every month or once every three weeks for treatment, whatever their condition is. In some cases this procedure has been employed for two years.

CASE REPORTS

Eugene had a guilt complex; he washed his hands a lot and did a lot of praying; he would have spells of panic and think he was going to die or go crazy; and he was very nervous and sleepless. He was in the hospital for several extended periods undergoing electric shock treatment. During one period he sought solace in alcohol; we tried to shift to sedatives, but Eugene was apt to drink the whole bottle of sedative at one time.

Finally we came to the point where we were giving treatments periodically, perhaps once a week to start, once every two weeks, then every three or four weeks.

His mother died in the meantime, but first she had a fracture of the hip, was in bed for many months, finally had strokes and died. Then there was an unfortunate love affair.

Eugene has now been working regularly for a couple of years. How long have you been working?

PATIENT: About 17 months.

DR. ALFORD: Instead of spending money he has been earning money and helping the family out. How are you getting along, Eugene?

PATIENT: Very well now, Doctor, I believe.

DR. ALFORD: Are you sleeping well?

PATIENT: I don't have any trouble sleeping at all. I sleep very well.

DR. ALFORD: No more drinking?

PATIENT: No, no more drinking, none whatsoever.

DR. ALFORD: Not very much praying?

PATIENT: Not so bad; I don't pray nearly so much any more.

DR. ALFORD: Next is Martin. The Nazis got after Martin. They first closed in on him in a New York hotel and there was quite a commotion. He got home and had several courses of electric shock therapy, but the idea kept coming back. Finally we switched to the method of staggering treatments. You get one every three weeks?

PATIENT: Every month, now.

DR. ALFORD: He was in a war plant at that time. When that closed down he went to work as a draftsman, and practically ever since the close of the war you have been a draftsman?

PATIENT: Since I left the university. I was trained in the university as an architect.

DR. ALFORD: How long is that?

PATIENT: I graduated in 1936.

DR. ALFORD: Since the war you have been working with private firms?

PATIENT: Yes, a couple of years.

DR. ALFORD: You are working regularly?

PATIENT: Yes, working every day, five days a week.

DR. ALFORD: Do you feel pretty well?

PATIENT: I am feeling a lot better.

DR. ALFORD: You have been feeling better the last two or three months?

PATIENT: That is right.

DR. ALFORD: I do not think this procedure of staggering treatments is altogether a temporizing one. I think it may be one method of approach. I recall one case that I was very worried about in which a voice—an auditory hallucination—persisted. Despite courses of electric shock, the girl could hear this whisper all the time.

In desperation I put her on these staggered treatments for several weeks, then every two weeks, then every three weeks, and after about eight or nine months, to my delight, she told me one day she had not heard the voice for a couple of weeks. Now the treatments have been discontinued altogether.

In conclusion, electric shock therapy, I believe, is a great boon in the care of the psychoneurotic patients and even has brought relief to otherwise incurable cases. I also think it is possible that the method of staggering treatments in the form of out-patient treatments is perhaps a useful approach.

SCIENTIFIC EXHIBIT

Glomerular Nephritis; Recognition and Treatment

FRED I. GILBERT, JR., M.D., AND L. MARTIN GRIFFIN, JR., M.D.

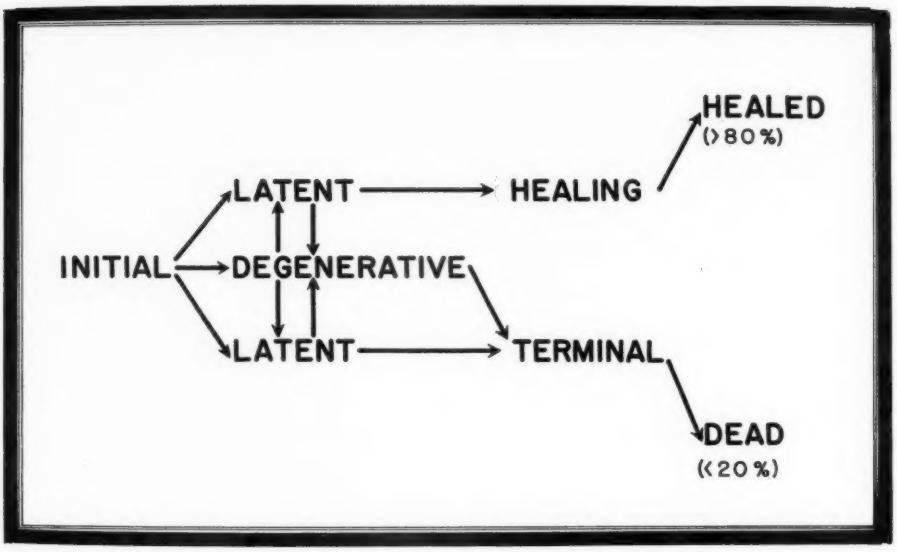
DEPARTMENT OF MEDICINE, STANFORD UNIVERSITY SCHOOL OF MEDICINE, SAN FRANCISCO

ALTHOUGH we know little of the prevention of glomerular nephritis and have only hypotheses as to its pathogenesis, it is nevertheless true that some progress has been made in the recognition and management of the various stages through which the disease develops.

Treatment of glomerular nephritis involves imposing the least possible work on the damaged kidney. Experimental and clinical evidence indicates that when a large number of nephrons have been rendered wholly or in part functionless, a reduction in the osmotic work of the kidney decreases uremia, anemia, hypertension, and proteinuria. Reducing the renal work is accomplished by decreasing the protein intake to a low but adequate level.

The diagnostic and therapeutic principles included in this exhibit are those that have been developed and put into practice by the group engaged in the study of Bright's disease at the Stanford University School of Medicine.

Medical illustration: Kay Hyde, V. A. Hospital, San Francisco. Drawings of casts by Dr. Kirk Stevenson, Stanford University. Photographs of certain tissue sections from "The Renal Lesion in Bright's Disease," Addis, T., and Oliver, J.; P. B. Hoeber, New York, 1931; and other data from "Glomerular Nephritis, Diagnosis and Treatment," Addis, T., The Macmillan Company, New York, 1948.



DEFINITION

A pan-nephritis believed to be caused by an antigen-antibody reaction following an infection by hemolytic streptococci, and characterized by a changing clinical picture dependent on the progression of the glomerular, tubular and interstitial lesions.

INCIDENCE

Less than 1% of patients with hemolytic streptococcal infection will develop glomerular nephritis. Abrupt onset of glomerulitis occurs within one month after infection. Seventy per cent of cases are between the ages of 5 and 20 years, although no age group is spared.

Of those patients developing glomerular nephritis, over 80% will undergo healing. Of these, 80% will be healed in two years; the remainder within ten years.

CRITERIA OF HEALING

1. Absence of red blood cells in acid, concentrated urine.
2. Less than 200 mg. proteinuria per 24 hours.

DIAGNOSTIC STEPS TAKEN WHEN PROTEIN IS FOUND IN THE URINE

A thorough history and physical examination should precede any laboratory investigation.

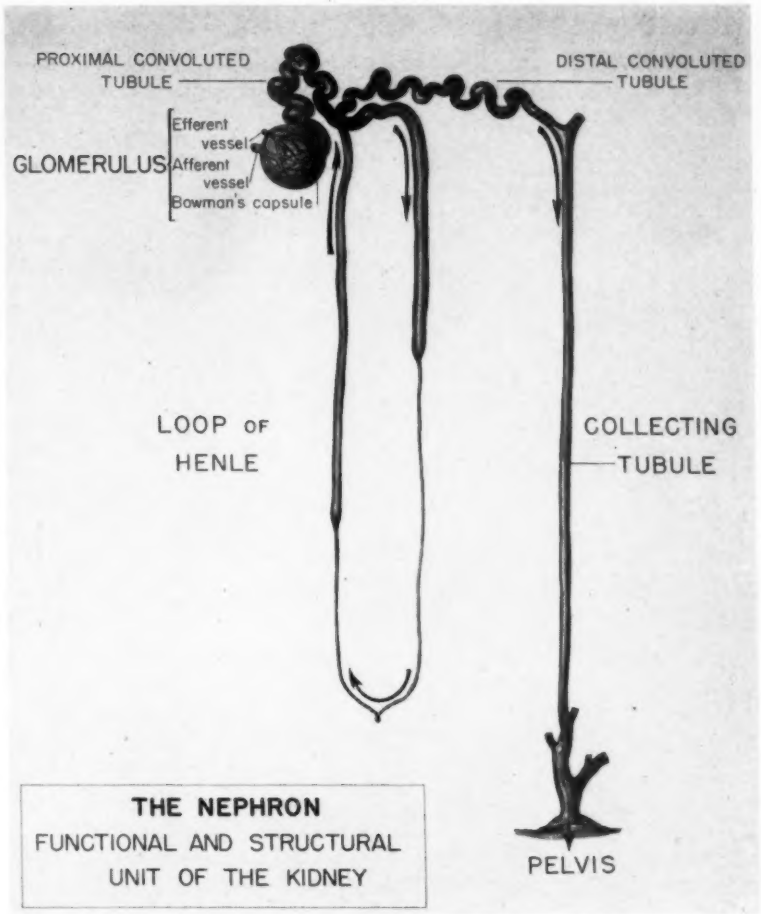
1. Repeat urinalysis with sediment study on a fresh specimen (formed elements, cells, bacteria).

Blood studies include white cell count, packed cell volume, sedimentation rate, and serum creatinine.

2. Appropriate bacteriologic studies, depending on clinical picture and sediment.

3. If serum creatinine is less than 3 mg. per cent, concentrate the urine for a twenty-four hour protein excretion, and an Addis count of cellular elements and casts. If creatinine is greater than 3 mg. per cent an attempt to concentrate urine will cause an increase of uremia.

4. If urinary findings, history, and physical examination suggest lesion other than glomerular nephritis, residual urine and excretory urograms may be done to aid in the exclusion of neoplasms, congenital anomalies, and chronic pyelonephritis. Cystoscopy and retrograde pyelography are done if necessary.



COURSE

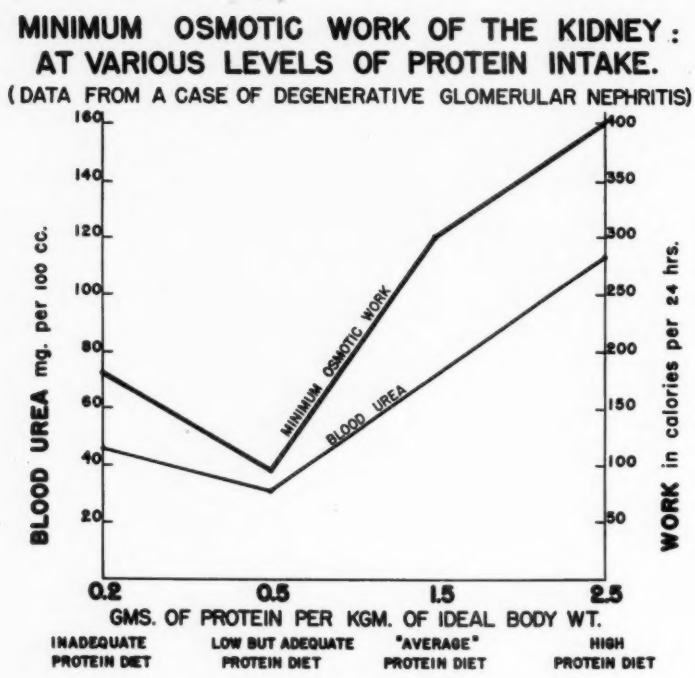
The patient who contracts glomerular nephritis may pass through the following stages:

INITIAL (Acute) STAGE: Is the abrupt onset of glomerular nephritis, but this stage is *usually unrecognized.*

Initial lesion rapidly subsides and patient usually passes into the asymptomatic LATENT STAGE.

A small percentage pass into the DEGENERATIVE (Edematous) STAGE, readily recognized by patient and doctor.

As the lesion progresses and the number of functioning nephrons decreases, the patient gradually slips into the TERMINAL STAGE.


MINIMUM OSMOTIC WORK OF THE KIDNEY: AT VARIOUS LEVELS OF PROTEIN INTAKE.
(DATA FROM A CASE OF DEGENERATIVE GLOMERULAR NEPHRITIS)
BLOOD UREA mg. per 100 cc.
WORK in calories per 24 hrs.
MINIMUM OSMOTIC WORK
BLOOD UREA
0.2
0.5
1.5
2.5
GMS. OF PROTEIN PER KGM. OF IDEAL BODY WT.
INADEQUATE PROTEIN DIET
LOW BUT ADEQUATE PROTEIN DIET
"AVERAGE" PROTEIN DIET
HIGH PROTEIN DIET

MINIMUM OSMOTIC WORK OF THE KIDNEY AT VARIOUS LEVELS OF PROTEIN INTAKE

It will be noted that blood urea and osmotic work increase directly with the protein intake, except where an inadequate protein diet results in increased catabolism of body protein.

(Data from a case of degenerative glomerular nephritis)

TREATMENT

RATIONALE OF LOW BUT ADEQUATE PROTEIN DIET

Allowing the diseased kidney to rest is the most effective therapy. This is accomplished by reducing osmotic work. The minimum osmotic work (W) of the kidney in excreting each urine solute for 24 hours is expressed in the formula:

$$W = NRT \left[\ln \frac{U.C.}{B.C.} - \left(\frac{U.C.-B.C.}{U.C.} \right) \right]$$

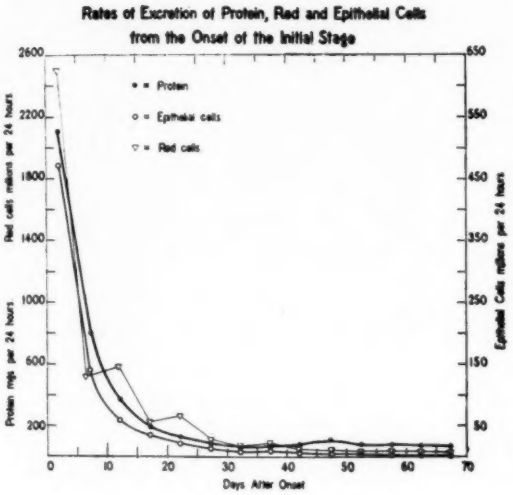
Where N = Rate of excretion in gram mols. / 24 hours.
R = Gas constant.
T = Absolute temperature.
U.C. = Urine concentration of solute.
B.C. = Blood concentration of solute.
W = Work in calories / 24 hours.

Therefore urine solutes with high excretory rate (N), and a high $\frac{U.C.}{B.C.}$ ratio require considerable work to excrete. *Urea is the only solute where both conditions exist.*

THERAPEUTIC CONCLUSIONS

1. Urea excretion should be kept at a minimum by adequate low protein diet.
2. Urine should be kept dilute at all times.

THE REST TREATMENT OF GLOMERULAR NEPHRITIS


Rates of Excretion of Protein, Red and Epithelial Cells
from the Onset of the Initial Stage
• = Protein
o = Epithelial cells
▽ = Red cells
Red cells millions per 24 hours
Protein mgs. per 24 hours
Epithelial Cells millions per 24 hours
Days After Onset

Initial Stage

Bed rest, at least one week.

Low protein diet (most important during this stage as reducing the excretory work may permit recovery of a larger number of nephrons than would occur with high protein diet).

Latent Stage

Low protein diet as long as active disease continues (or longer because of nephron loss). Lead normal life.

Calculation of Adequate Low Protein Diet

Adults: Give ½ gram of protein per kilogram of body weight daily, plus protein lost in urine per 24 hours.

Children: ½ to 1 gram of protein per kilogram of body weight daily, plus protein lost in urine per 24 hours.

Degenerative Stage

Low protein diet, plus protein lost in urine.

Salt restriction to reduce edema.

Periodic relief of symptomatic effusions by paracentesis, thoracentesis; Southey tubes where edema fluid is mobile.

(Large amounts of serum albumin or plasma intravenously induces diuresis in many patients, but causes only transient rise in plasma proteins. Other diuretics may be harmful.)

Terminal Stage

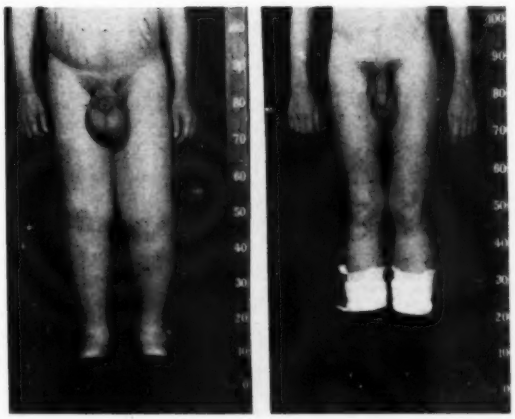
Low protein diet.

Increase salt (depending on cardiac status) to prevent dehydration.

Replace loss of fixed base.

Transfusions for symptomatic anemia.

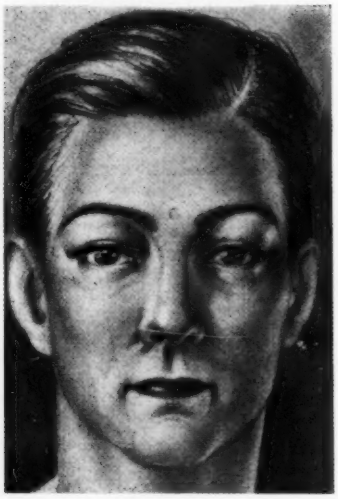
Terminal symptomatic care.



Patient in degenerative stage of glomerular nephritis with massive mobile edema. Southey tubes inserted in distended tissues of legs resulted in loss of 8,500 cc. of fluid in six hrs., 48 lbs. weight loss in five days.

CLINICAL PATHOLOGICAL STAGES

INITIAL STAGE



Symptoms and Signs

Abrupt onset of Coffee- or red-colored urine. Moderate hypertension. Brawny edema.

Appearance of Urine

Opaque brown or red.

Urine Protein

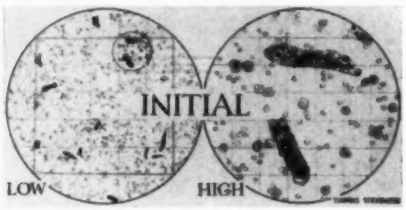
Proteinuria of 0.2 to 3.0 gm./24 hours.

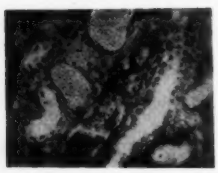
Hemo-Chemical

Serum creatinine elevated. Mild anemia and hypoproteinemia (due to increased blood volume?). Leukocytosis. Rapid sedimentation rate.

Renal Function

Moderate to severe temporary impairment due to blockage of large number of glomeruli.





Most Important Sediment Findings

Red cells, red cell casts and many tubule cells.

Pointer indicates red blood cell cast in lumen of tubule. Above are fresh RBC within tubules.

LATENT STAGE

Symptoms and Signs

The only abnormalities found in this stage are in the urine.

Asymptomatic.

Appearance of Urine

Clear.

Urine Protein

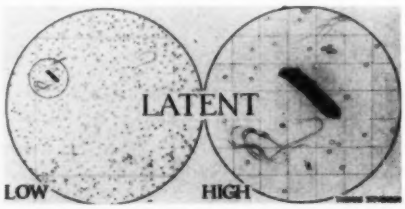
Usually less than 0.5 gm./24 hours.

Hemo-Chemical

Serum creatinine usually normal. No anemia, leukocytosis. Plasma proteins normal. Sedimentation rate usually elevated.

Renal Function

May have 10-60% reduction in function due to irreparable loss of nephrons.

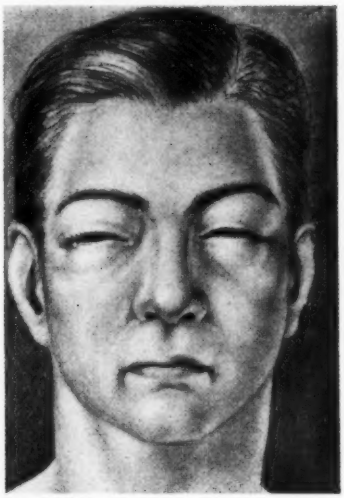


Most Important Sediment Findings

Persistent microscopic hematuria and red cell casts.

OF GLOMERULAR NEPHRITIS

DEGENERATIVE STAGE



Symptoms and Signs

Feels well except for pitting edema of ankles and face at onset; later may develop mechanical discomfort from ascites, hydrothorax.

Appearance of Urine

Clear, foamy.

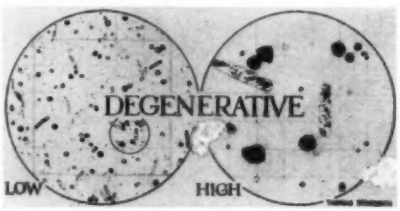
Urine Protein

Marked proteinuria of 5 to 50 gm./24 hours.

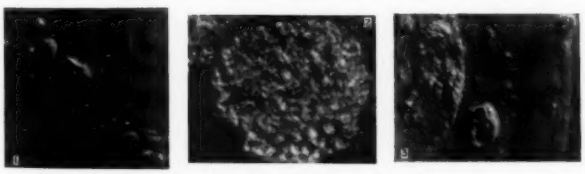
Hemo-Chemical

Serum creatinine normal at first. Hypoproteinemia. Lipemia with elevated blood cholesterol.

Renal Function Decreasing renal function.



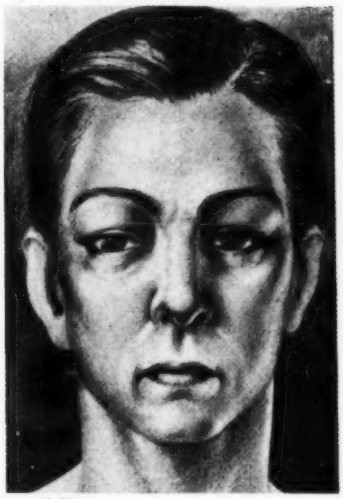
Phase microphotograph. *1. Hyaline cast with fat and epithelial cell inclusions. 2. Epithelial cell filled with fat. 3. Hyaline cast. Tubule cell.*



Most Important Sediment Findings

Droplets of fat in casts, in epithelial cells and free in the urine. Microscopic hematuria.

TERMINAL STAGE



Symptoms and Signs

Development of fatigue, nausea, vomiting parallels increasing uremia with anemia, hypertension.

Appearance of Urine

Pale, clear.

Urine Protein

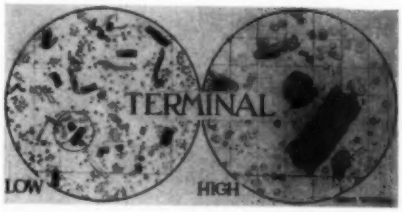
Moderate proteinuria of 3 to 15 gm./24 hours.

Hemo-Chemical

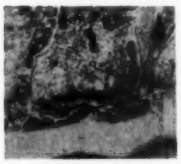
Serum creatinine high. Increasing anemia. Low or normal plasma proteins (5 gm.).

Renal Function

Majority of nephrons destroyed, deepening uremia.



Fragile renal failure cast. Broad casts in ducts of Bellini at entrance to renal pelvis.

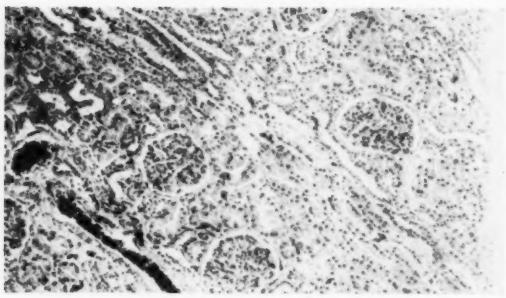


Most Important Sediment Findings

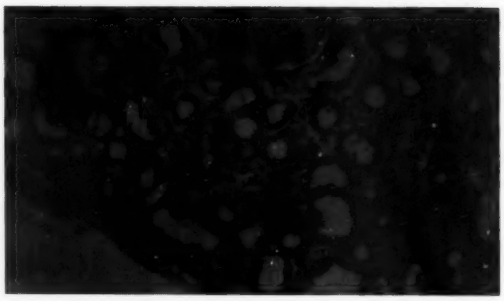
Even with dilute urine, RBC are found. Number and breadth of broad casts increases with slightest dehydration.

TISSUE SECTIONS

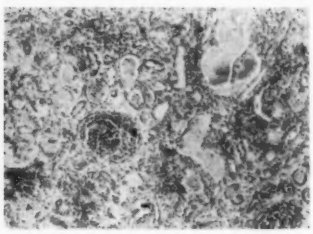
In all stages of glomerular nephritis, the clinical picture equals the sum total of the interdependent glomerular, tubular, interstitial and vascular lesions.



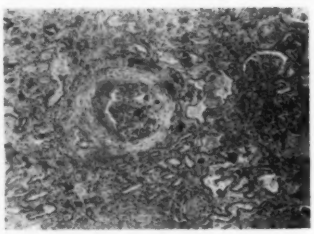
Normal—Kidney section showing normal cyto-architecture of glomeruli, tubules, interstitial tissue and vessels.



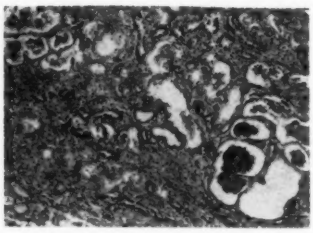
Degenerative stage. Sudan stain shows much fat in tubule cells.



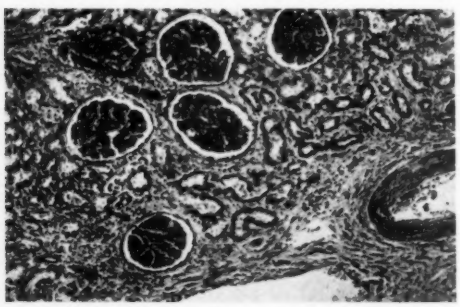
Expired during initial stage. Stormy clinical course with death one month after onset. Age 5. Striking epithelial crescent in center of field, tubular atrophy and dilatation, and granulocytic infiltration are compatible with the short clinical course.



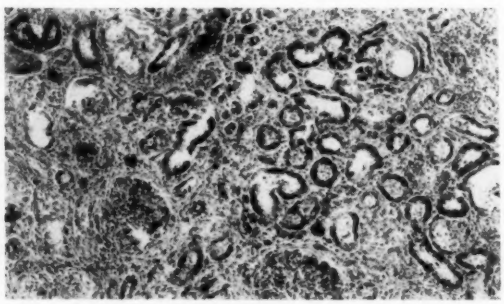
Expired in terminal stage. Age 38. Many shrunken, fibrotic glomeruli, glomerulus with extreme pericapsular fibrosis, epithelial crescent and fibrotic tuft, alternating tubular dilatation, interstitial scarring and arterial thickening.



Terminal stage. Extreme cyst-like dilatation of tubules alternating with atrophied or compressed units, possibly due to interstitial scarring.



Expired during latent stage. Age 45. Only evidence of renal lesion is cellular increase in glomerular tufts, some cortical scarring and intimal thickening.



Expired at end of degenerative stage. Kidneys large and smooth. Dark tubule cells and some glomeruli contain much fat. Age 45.

The Medical Bookman

PHYSICAL MEDICINE IN GENERAL PRACTICE*

This is the second edition of Dr. Bierman's important work on physical therapy in medical practice. World War II demonstrated effectively the value of physical methods in medical and surgical practice with rehabilitation on a large scale in speeding the recovery of the wounded and those ill from other causes. Dr. Bierman has included this valuable material in his new edition and has added a chapter on specific problems of rehabilitation which are of interest to the medical practitioner. There is still relatively little general use of these extremely valuable adjuncts in aiding people to recover from disease and injury, and with the new emphasis upon early ambulation in both surgery and medicine, this phase of practice is increasingly important. A book such as this naturally then becomes important to the general physician who would keep himself and his practice in accord with the most modern thought. The organization of the subject matter and the approach to it is everywhere kept within the viewpoint of the general practitioner.

Heat and cold are still the most widely used physical agents, and the most valuable. A considerable proportion of this book is devoted to these agents. "The skin may be considered as an organ which lies between the interior of the body and its environment. . . . The blood vessels of the skin form a large reservoir capable of holding about one quarter of the total blood volume, which increases or diminishes markedly in accordance with local and general needs. . . . Changes are also brought about through the action of nerves and nerve endings, lymph channels, sebaceous and sweat glands, and by metabolic responses, such as pigment formation and production of vitamin D. . . . These and other changes occurring in the skin are of particular importance in explaining the therapeutic value of many physical procedures whose influence is completely or mainly limited to the integument."

The author further discusses the use and effectiveness of heat and cold when applied to various parts of the body and the specific uses to which they can be put. The anesthetic effect of cold is pointed out, as well as possible dangers which it may cause. Particularly dangerous, of course, is the use of the ice bag in abdominal pain liable to be caused by an inflamed appendix, when the diminished sensitivity may cause a false sense of security, while the infection proceeds to a dangerous point. Also mentioned is the shocklike condition produced on some people by immersion of even the hands in cold water, with actual syncope at times. The use of cold to diminish the blood needs of extremities in which the circulation is impaired by injury is discussed. Indications, value, and technic of heat application is also effectively presented.

Hydrotherapy, both local in the recovery and rehabilitation of injured extremities, and general in more widely spread muscular damage such as that from poliomyelitis, is the subject of an entire chapter. Typical of the author's attention to practical detail is the description of the lowly Sitz bath, a most effective form of relief in the ever-present ano-rectal disturbances, and the continuous hot compresses in treating infections of the skin and subcutaneous tissues.

The effect of climate upon health is the subject of a chapter, including the various physiologic effects produced by heating and chilling. Of climate in general, the author states: "The most beneficial influence of climate would be secured when living

*Physical Medicine in General Practice. By William Bierman, M.D. (With a chapter on medical rehabilitation by Sidney Licht, M.D.) 686 pages. 1948, Paul B. Hoeber, Inc., New York. Price $8.00.

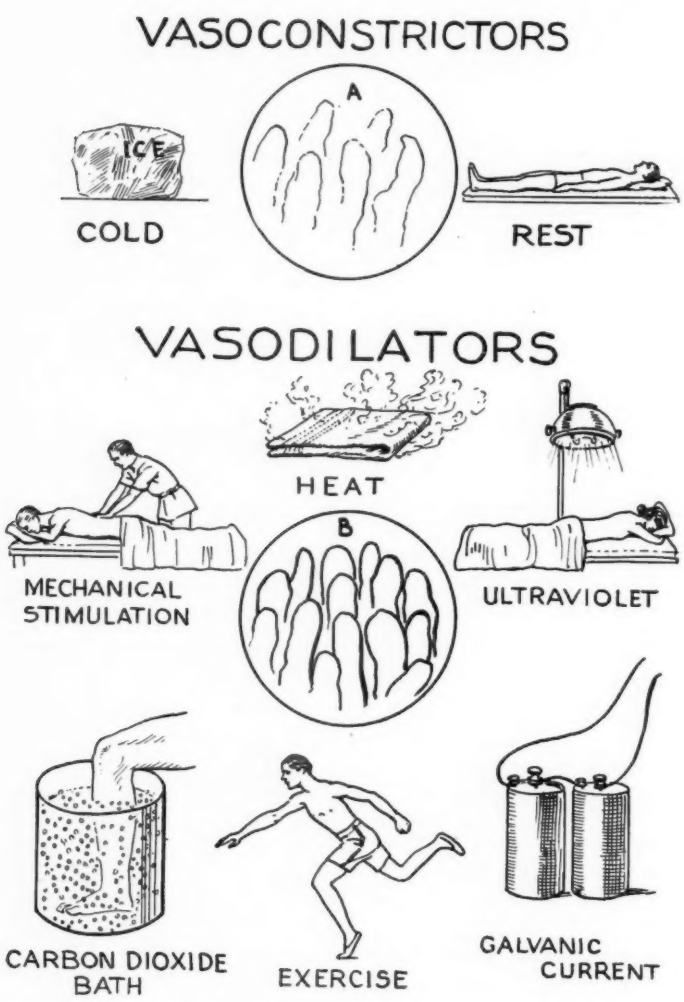


Figure 1. Physical agencies causing vasoconstriction and vasodilatation. A. Constricted capillaries. B. Dilated capillaries (schematic). (Illustrations from Bierman: *Physical Medicine in General Practice.*)

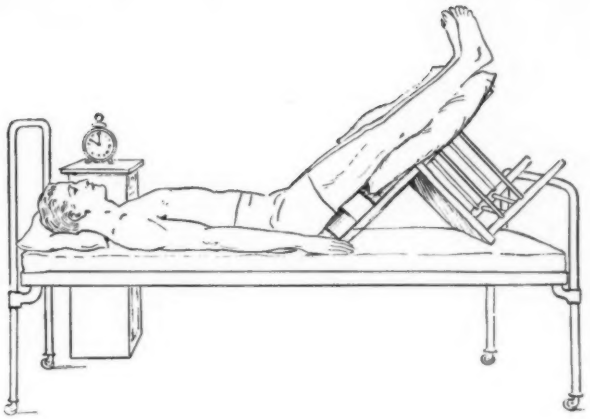


Figure 279. Buerger exercises. Position A: Legs held elevated.

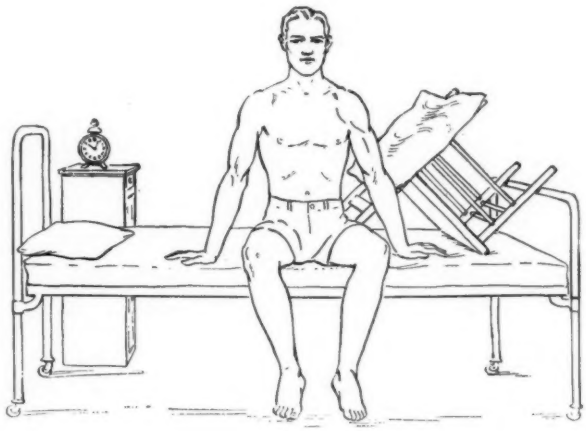


Figure 280. Buerger exercises. Position B: Patient sitting on edge of bed.

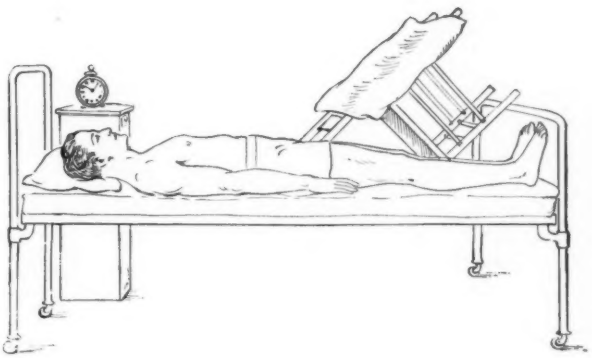


Figure 281. Buerger exercises. Position C: Patient lying flat on bed.

outdoors in a comfortable environment wearing little, if any, clothing." He continues to point out that climate has largely been discarded as a factor in the recovery from tuberculosis and that the high, dry climate formerly favored may actually be dangerous because of oxygen lack. Continuing further, the author discusses the beneficial effect of rest and change in spa therapy upon nervous tension disorders, probably the greatest benefit that climate has in treating human ills. In concluding this chapter, the attributes of most well known American Spas are mentioned.

Many of the muscular strains which come to the general physician are markedly benefitted by "baking" with radiant heat, and since high pressure instrument salesmen are always waiting to place expensive instruments with the unwary physician, Dr. Bierman's advice in regard to this form of treatment is valuable. "The carbon filament lamp, modest though its appearance and price, lowly though its position (from the medical practitioner's point of view because it is offered for sale to the layman by druggists, hardware and department stores), is none the less an extremely useful instrument. It deserves a place in every doctor's office, in every hospital, and for that matter in every home, because of the numerous conditions in which it may be of service. . . . Deserving of extensive use in the physician's office and in the hospital is the tungsten filament lamp which is comparatively richer in visible radiation and emits a far whiter light because of the metal used in it." The dangers of this form of treatment are also described, something which every physician using any physical method must keep constantly in mind.

Diathermy, both the long-wave and the more frequently used short-wave forms, has proved of much value in treating a widely varied number of conditions. A great deal of misconception seems to exist in regard to its beneficial effects and Dr. Bierman says: "Whether or not any effect other than of heat is produced on animal tissues by the short wave current is a contraversial question. . . . The opinion held today is that a special non-thermal effect is not exerted by the short wave current." Keeping this in mind, it is obvious that for many of the conditions treated by the general physician, such expensive machines are neither necessary or safe, and Dr. Bierman says further, "Short wave diathermy should not replace simpler forms of heating that are equally effective." The chapters on diathermy, however, are complete and authoritative for those who need to use this method.

"Give me power to produce fever, and I will cure all disease," an aphorism attributed to Hippocrates, is quoted in the opening of a chapter on Fever Therapy. Various methods of producing temperature elevation as a therapeutic measure are discussed, but with the diminishing need for fever therapy in venereal disease and the expense and special knowledge required to apply it, the general physician will probably not be much concerned with this form of treatment. There is an excellent chapter on Fever Therapy, however, as well as on Surgical Diathermy and the use of the Galvanic Current in the diagnosis of nerve injuries and in stimulation of activity in muscles during nerve regeneration.

Perhaps no form of physical therapy is more widely misused than heliotherapy, both by exposure to the sun and with ultraviolet lamps. Its use has been shown in many cases to be positively dangerous for the tuberculous and this is sometimes true of other conditions. As to the actual value of ultraviolet radiation, there is considerable difference of opinion and perhaps the simplest and most effective answer is Dr. Bierman's: "After ultraviolet radiation the patient has a healthier appearance; his skin has a better texture; his muscles are firmer; psychologically there is no doubt that a person who can see a mild erythema and subsequent pigmentation of his skin feels better because of his healthful appearance."

An important physical measure often overlooked by the general physician is massage. This is particularly true, also, since the newer work on emotional influences in psychosomatic medicine has shown the importance of the physician-patient relationship in psychotherapy. Dr. Bierman says pointedly: "The psychological factor of which many physicians are probably unaware, offers an explanation for the widespread activities of irregular practitioners. The physical 'laying on of hands' has a reassuring value, even though these hands

be not guided by honest and scientific reason." And in view of the widespread use of massaging machines in beauty parlors and the extravagant claims made for them it is interesting that "Contrary to popular belief, massage does not directly increase muscle power nor does it remove fat. When Rosenthal massaged the abdominal walls of animals with sufficient vigor to produce multiple hemorrhages, destructive changes in adipose tissue were not observed."

"Rehabilitation should begin as early in convalescence as the course of the disease will permit, but too often in the past a well intentioned caution on the part of the physician has delayed its commencement beyond the point of maximal advantage," states Dr. Sidney Licht in his excellent chapter on Medical Rehabilitation.

The tremendous value of early rehabilitation with graduated exercises and occupational therapy was so well demonstrated by our experience during the recent war that every physician should familiarize himself with what can be accomplished and, more important, the extreme importance of beginning early, before unsatisfactory habit patterns are formed. As Dr. Licht says: "Medical rehabilitation will increase in importance with the passage of time if for no other reason than that it will eventually save the community and the state much money which would otherwise be spent in unemployment benefits, insurance compensation, and custodial care." This one chapter will be well worth the price of the book to the average physician, if it enables him to get both surgical and medical patients back to normalcy in a shorter period of time.

"The physician assumes legal responsibility when he treats patients by physical agents just as he does when he employs chemical agents. He must therefore exercise reasonable professional care in the treatment of his patient. This includes taking a history and making a physical examination. When an unusual form of treatment is used the physician assumes an additional risk because, if any accident occurs, the plaintiff may contend that this ministration differs from accepted practice." This statement should give pause to those using physical therapy instruments with which they are not wholly familiar and points up again Dr. Bierman's often repeated thesis that the simplest form of physical therapy is the best.

THE LAST third of the book deals with specific disease conditions in which physical therapy is of benefit, with a discussion of the type of treatment liable to prove most effective in each. Indicated procedures are given in detail as to technic, including the exercises, etc., necessary for rehabilitation. Dr. Bierman also points out the importance of such treatment in the neuroses which constitute approximately half of medical practice with: "For neurotic and psychically disturbed patients, physical procedures are of value not only because of the physiological changes which they induce, but also because of their psychological influence. Weir Mitchell first called attention to the fact that neurotic patients require a definite treatment regimen of rest, dietary advice, and physical therapy."

Physical Medicine in General Practice is a complete and authoritative book on this important subject. It deserves study by all those who plan to use physical methods, which in the essence means every physician, for modern experience has shown that proper rehabilitation is as important as any other form of therapy in the treatment of both medical and surgical conditions.

F. G. S.

MEN OF MEDICINE

Lahey, Perfectionist

FRANK HOWARD LAHEY, distinguished surgeon, founder and driving force of the Boston clinic that bears his name, is a perfectionist. His colleagues recognize the fact, and his friends—whether trying to match his mid-eighties score on the golf links or participating in field trials of hunting dogs—confirm the diagnosis. Psychologists and psychiatrists have made us wary of the term, but Dr. Lahey exemplifies that rara avis a perfectionist who constantly drives himself and his staff to new heights of excellence, and yet remains disciplined, controlled, without frustration or inner struggle. He is a man confidently working in one direction, devoted to the clinic and its ever increasing usefulness, devoted to his wife, content with a strenuous regimented routine. He is a man who lives the life he wants, is convinced of its worth, has fun doing it!

Such inner peace results from a combining of many qualities, among which courage and clear-headedness are outstanding. It took extraordinary courage for young Francis Lahey (disliking the baptismal form of the name he changed it to Frank during his Harvard student years) to reject the place long prepared for him in his father's bridge building firm, and to pursue his determination to become a surgeon. The decision was the more difficult because the construction firm of Fletcher and Lahey was prosperous, well respected, ready for the sons of both partners to carry on what their fathers had so ably initiated. Moreover Frank had definite engineering ability. Against all that, he could offer only the unsubstantiated conviction that he wanted to be a surgeon. He couldn't argue his case logically; he didn't know why. Probably modern vocational experts who maintain that both surgeons and engineers need the quality of "structural visualization" would assure him that surgery has effectively utilized his native ability. And no one who observes the precision and efficiency with which the clinic is run could deplore that his business talents have not found an outlet.

After the event, it is easy to rationalize, and today Dr. Lahey generously attributes his interest in surgery to Dr. Charles Benson of his home town, Haverhill, Massachusetts. He was, says Dr. Lahey, "a man well trained and well in advance of his time . . . with whom I was closely acquainted and whose work I watched before studying medicine."

He took his M.D. degree at Harvard Medical School in 1904, thereafter serving as intern and house surgeon at Long Island Hospital. From 1905 to 1907 he acted as surgeon at the Boston City Hospital, and later at the Haymarket Relief Station. In 1908 he was appointed Instructor in Surgery at Harvard, and continued to hold positions there until he changed to Tufts Medical School, where he became Assistant and then full Professor of Surgery, a place he held, with time out for service at Camp Green and overseas during World War I, until 1917. On his return from France he was made Professor of Clinical Surgery at Harvard with teaching in the Boston City Hospital.

He was still a very young man, he had vindicated his choice of profession, he was doing extremely well. But boyish-appearing Dr. Lahey had experienced enough of two kinds of medical practice to feel stirring within him that urge to perfection that is still characteristic of him at sixty-seven. He had been accustomed to spending part of his day operating at City Hospital on charity patients, i.e., on X23, Z7, Y46. Then another part of the day he would spend working with private patients, Maribel Knox, Arthur Sinton—real people, individuals recognized as such, deserving of the encouragement and the help that can flow

FRANK HOWARD LAHEY

SARA M. JORDAN, M.D.

from the doctor-patient relationship. Worried young Dr. Lahey wanted all his patients to be individuals with names, not anonymous cases with numbers. Moreover he realized that sick people usually need more complete care than any one man, no matter how humanly sympathetic or how talented, can give them. And so, tentatively at first but with high hope and firmly rooted ideals, the idea of the clinic evolved.

Sitting in his modestly furnished but attractive office at the clinic today, overlooking the stream of traffic on Boston's Commonwealth Avenue, Dr. Lahey may disclaim all knowledge of how it really got under way, how it grew so amazingly that the original building erected on the present site in 1926, was doubled in 1933, again doubled in 1939, and is currently once more being enlarged. He may say that he just can't account for how it all happened, but he remembers the courage it took to resign a Harvard professorship for a dream of increasing the numbers of sick people who could be treated sympathetically as human beings, and yet who would have at their service the complete care of a staff of skilled experts.

His own role Dr. Lahey sums up in the sentence: "I am a fairly good surgeon and not much else." But those who know attribute a large part of the clinic's success to the personality of its founder. One of those who has most reason to know is Dr. Sara Murray Jordan, the charming gray-haired woman who is chief gastroenterologist at the clinic. As a young medical student at Tufts she had done metabolism work for Dr. Lahey when he was a professor there, and when the idea for the clinic finally took shape she was asked if she'd like to continue it with the new group that was being formed. She became a part of that nucleus that included, along with herself as youthful pinch-hitter, Dr. Lincoln Fleetford Sise, anesthetist, and Dr. Howard M. Clute, an assistant until 1935. Her recollections of those early days are full of Dr. Lahey's inexhaustible kindliness particularly toward the very old and the very young.

"My daughter, who's grown up now," Dr. Jordan inclined her head toward the silver-framed portrait of a handsome young woman, "says she has never known greater gentleness than Dr. Lahey's when he treated her for swollen glands when she was four. Sometimes I was afraid that his kindness would lead patients into speaking of him without the respect he deserved. I remember I once reproached an old woman for saying to me, 'Lahey doesn't think so.' When I frowned at her disapprovingly, she said indignantly, 'Well, I don't say Mr. Shakespeare, and I guess that they're both tops.' "

And if Dr. Jordan's affectionate respect for her friend, guide, and chief was deeply rooted, Dr. Lahey's respect and admiration for her ability took definite form. Twenty years ago he had her treat him for stomach ulcer, observing the rules so meticulously that he even drank milk while operating. It was only when he went up to Rockport for a recuperative vacation after the peptic ulcer had healed that he found occasion to remonstrate with his doctor. Having played eighteen holes of

golf the first morning, he dragged back to the club house limp and perspiring. "Say, do you realize how weak people are after your treatment?"

As a matter of fact it speaks well for both doctor and treatment that the patient suffered no recurrence, not even in the clamor and strain of wartime Washington in the early 40's where Dr. Lahey was chairman of the Service for the Procurement and Assignment of Medical Personnel for all of the Armed Forces. Indeed, being by temperament and training an essentially controlled and disciplined person he actually throve on the overwork that drove most men into fury and frustration. He sums up his notable achievement with characteristic, dry brevity. "With the aid of the other members of this board, Drs. Harvey Stone, Harold Diehl, Willard Camalier, and James E. Paullin, [we] organized, set up, and oversaw the program for obtaining medical personnel for the Armed Forces without unduly dislocating medical care." So competently did he handle this task that he was also appointed chairman of the Medical Consulting Board of the U.S. Navy in which capacity he "visited and inspected nearly every naval institution maintained by the U.S. Navy" with special emphasis on "inspection tours in the Pacific before many of the large undertakings" in the Pacific theatre of war. As an additional duty he and his clinic trained large groups of Navy surgeons in the use of spinal anesthesia.

As it happens Dr. Lahey is an experienced and enthusiastic traveler, making use of all known methods of transportation but delighting particularly in airplane travel. Often he utilizes necessary trips not only for relaxation—he has trained himself to be able to fall asleep at a moment's notice—but to enjoy the companionship of his beloved wife, Alice, with whom his relationship is devoted and tender. They have no children, a matter of regret to both of them, though perhaps that very lack has resulted in a greater closeness between them. They share too a love of simple living and of the out-of-doors that finds expression in their trips to their cottage on Lake Winnepesaukee, New Hampshire. As a part of the Bald Peak Colony Club there are opportunities for swimming, fishing, golf, and for tramping the woods and fields with dogs and gun in search of grouse, woodcock, or pheasants. Even in winter, if the doctor has a report to write or a deadline on an article to meet, they may drive up to the well insulated cottage for a happy and companionable weekend, far from the never-ceasing demands and responsibility of the clinic and of his position as Chief of Surgery at the New England Baptist Hospitals. Ordinarily he performs a thousand of the clinic's ten thousand annual operations. War duties cut into his time seriously enough to reduce that number by three or four hundred. Dr. Lahey is a busy and important man. He knows it, but he hasn't been spoiled by it.

Let an anecdote of the doctor's own choosing illustrate the point.

"When Mrs. Lahey and I were going to Honolulu on a vacation before World War II, the American College of Surgeons, ascertaining that I was going, asked me to inspect the Queen's Hospital as to whether or not it could be classified as Grade A qualification, which I agreed to do. I went to Queen's Hospital and saw the medical director, Dr. Niles Larson, looked the hospital over, looked the records over and approved thoroughly of it. Following this Dr. Larson said that there was a surgeon of German extraction in the operating room, operating on a patient for gallstones, and that I would probably be interested to go up and see him do it. Dr. Larson stated that he could not go with me but sent a nurse up with me. The nurse dressed me in a cap and gown, opened the door, I went in and she stayed out. The doctor who was operating had a number of visitors; he looked up and no one introduced me and so I introduced myself by saying, 'I am Dr. Lahey from Boston,' and the surgeon replied, 'Well, what of it?' It was an amusing and also a chastening incident."

Dr. Lahey's contributions to the progress of surgery have been varied and significant. Their worth is attested by the list of honors that have been bestowed upon him. He holds the Honorary Degree of Doctor of Science from Tufts College, from Boston University, from Northwestern University. In 1946 he was given the Medal for Merit by the Secretary of the Navy and the Certificate

of Merit by President Truman. From the American Gastroenterological Society he received the Friedenwald Medal, and from the Boston Surgical Society the Henry Jacob Bigelow Medal for accomplishments in surgery. It is that award that Dr. Lahey cherishes with special pride because it was given by his own confrères in his own town. Boston is not a town given to superlatives; Bostonians have an ingrained habit of weighing their words carefully. Therefore some of the remarks made upon the occasion of the presentation are well worth quoting.

> The award is made for "new and valuable work in surgery or in fields connected with it." The medal was first awarded in 1921 to Dr. William J. Mayo. Since then eight other awards have been made, this present one being the tenth. (The other recipients were Drs. William W. Keen, Rudolph Matas, and Chevalier Jackson, Mr. George Grey Turner, and Drs. John M. T. Finney, Harvey Cushing, Edward W. Archibald, and Allen O. Whipple. Surgeons of the United States, England and Canada are represented.)
>
> The Society has been chary about awarding the medal to one of its own members, and it can be accepted as fact that before doing so it has interpreted the terms of the award with more than usual stringency. In consequence, only one member has previously received the medal: Dr. Harvey Cushing.
>
> Tonight it gladly honors another member. Dr. Frank H. Lahey, director of the Lahey Clinic here in Boston, on the basis of his accomplishments not only in the field of surgery but also in those broader fields that are connected with it well merits inclusion in this distinguished group of recipients. His mastery of thyroid surgery and surgery of the esophagus and bowel, for example, is but an indication of the scope of his technical skill.
>
> The presidencies of the American Medical Association and the New England Surgical Society, the governorship of the American College of Surgeons and membership, both honorary and regular, in many other surgical societies point to his great influence among the medical profession. He has held professional posts in Harvard and Tufts College medical schools. The Lahey Clinic is famous for the opportunities it affords for graduate studies. Without his steadying influence during the war, the civilian physician situation would have been a serious menace to the public health. Even now, his influence is being continually exerted as a member of the Presidential Advisory Committee on the Integration of Medical Services in the Government to the end that, among other things, the veterans shall receive better care.
>
> Nor should we forget in honoring Dr. Lahey to do equal honor to Mrs. Lahey. All in this audience know what profound influence a surgeon's wife exerts on the surgeon. Without her sustaining aid his courage would many times falter; without her encouragement he would never be inspired to rise to heights believed by him to be beyond his reach. She puts up with long lonely hours, a frequently disrupted household and those temperamental peculiarities that are characteristic of a person who by nature and by training is above all things an individualist. Dr. Lahey will, I am sure, agree with me that without the devoted and loyal support given him by Mrs. Lahey he would never have achieved even a modicum of the deserved success that has been his.
>
> Dr. Lahey—superlative surgeon, doctor who teaches doctors, redoubtable administrator, adviser of Presidents in war and peace and, above all, a man who has the courage to be honest with himself—as the representative of the Boston Surgical Society I take great personal pleasure in having the honor to present to you in its name the Henry Jacob Bigelow Gold Medal.

There is in Dr. Lahey's office another symbol of achievement of which he is justifiably proud. It is a simply lettered framed certificate designating Frank Howard Lahey as an honorary member of the Royal College of Surgeons in England. His pleasure in being so honored was reflected by his colleagues in London when he delivered a lecture there before the College.

They were fortunate to hear him too, for in addition to having something important to say, Dr. Lahey has the even rarer gift of being able to say it well. He speaks in public with a briskly confident manner, a use of concise and telling phrase, with clarity and directness. The same qualities are evident in the informal summaries he gives for the instruction of students who are invariably present and as a matter of courtesy to the visitors attending his operations. Indeed a steady monologue accompanies his every action so that each operation becomes a lecture and a demonstration. Infinitely patient, gentle, painstaking, Dr. Lahey cares little for speed, never loses his nerve, becomes even steadier and calmer in moments of crisis. These

are more frequent than one might think, since Dr. Lahey is often called upon to correct earlier mistakes made by others, to act as a court of last appeal.

UNDERLYING the smooth precision of technic is a coordinated team work of which Dr. Lahey and the clinic are properly proud. Each operating team is a carefully drilled, thoroughly experienced unit capable of working together with the utmost professional accuracy. Always there is acting as anesthetist a trained M.D. who watches pulse, heartbeat, cyanosis, respiration—who quite literally holds a watching brief for the patient. Each assisting nurse is well trained, able. Anticipating Dr. Lahey's every need is his silent, dependable, perceptive operating nurse, Blanche Wallace. She has been with the doctor for twenty-four years, knows by a sure instinct developed in that long association, what instrument to place in his reaching hand. He may, perhaps, request a better light, ask for his magnifying spectacles that enlarge organs undergoing scrutiny two and one-half times. Doubtless it is this almost magical efficiency of the operating amphitheatre that makes an occasional blunder so glaring. With its perpetrator Dr. Lahey is bleakly pitiless. "You cannot afford to *think* something is right. You must *know*."

Dr. Lahey knows because he has observed, experimented, learned, remembered. And the thousands of anxious but hopeful souls who crowd the Commonwealth Avenue clinic year after year demonstrate their faith in his knowledge. Some of them are wealthy and famous, though neither their names nor their diseases would ever be divulged by any member of the clinic staff. Many who crowd the small waiting rooms or diffidently answer the summons of a nurse are poor people—Boston's poor, New England's poor. Indeed, one-third of the total volume is charity work. Very probably the charity patients too may be examined by Dr. Lahey himself. Sometimes, however, they don't know it; one woman complained bitterly that she had been seen only by subordinates. In the slight, quiet, blue-eyed, sandy-complexioned man who still looks far younger than his sixty-seven years she had not recognized "the great Dr. Lahey." Years ago there were even more serious penalties attached to his slender build and boyish appearance, for on one occasion a senior doctor declared that such a stripling was certainly too young to operate!

The convenient blanket title "head of the Lahey Clinic" covers a great many more duties than seeing patients and performing several hundred operations a year. Admittedly those functions serve the first aim of the institution, viz., to get people well, but Dr. Lahey visualizes other purposes, and all of them are materially advanced by his own activities. His design is fivefold:

I. We must get people well.

II. In getting people well, we must investigate and develop new methods.

III. We must train men in the new technics in order to perpetuate and to spread what we have learned.

IV. We must serve as an informal postgraduate center.

V. We must write and we must talk—with certain reservations. For we must keep still when we have nothing to say, and we must never create openings in order to satisfy our ego or for mere publicity.

Dr. Lahey has been particularly outstanding in investigating and developing new methods. Four operations have been named for him. His work in thyroid operations, together with the closely associated studies in metabolism and anesthesia, is world famous. His development of two-stage operations to lessen the shock of surgery to patients already dangerously weakened has been literally life-saving to hundreds. And he is constantly investigating, improving, discovering. One of the latest innovations in thyroid surgery is the preoperative use of the thiouracil compounds which often makes two- or three-stage operations unnecessary, and which cut the average hospital stay to about six days. Dr. Lahey and his clinic doctors (with an impressive history of some 27,000 thyroid operations out of which they lost only 100 patients) have also found that thiouracil or propylthiouracil will bring down the basal metabolic rate almost exactly one point per day.

To make new procedures, particularly surgical technics, available for teaching purposes, Dr. Lahey

has colored films taken of certain operations, thus coordinating his activities as operating surgeon and as instructor.

IN ADDITION to the fifty-three full time staff members of the clinic, among whom are Dr. Richard Cattell in general surgery and Dr. Gilbert Horrax, worthy successor to Dr. Cushing in brain surgery, there are some ninety fellows working and being trained. Eleven of these are working under five staff specialists in a special school of anesthesia. From it there are sent out all over the country remarkably well qualified young men to act as heads of departments in hospitals, medical centers, and institutions. They are products of Dr. Lahey's belief that an operating surgeon's mind and nerves may best be freed to deal with whatever emergency may arise by his working in unison with a skillful, conscientious anesthetist who acts as the patient's representative. So important does the doctor consider his anesthetists that in the recent remodelling of the building they have been given a room of their own for their paper work. And in the still compact and crowded quarters available that is a very real distinction!

To a perfectionist like Dr. Lahey the dream forever outruns actual accomplishment, but his ideal of having the clinic serve as an informal postgraduate center is a matter of solid fact amply attested by authority as outstanding as the American Medical Association. Incidentally, the doctor served a term as the Association's president beginning in the troubled and uncertain days of June 1940. He also served as president of the Interstate Postgraduate Medical Association of North America and of the American Association for the Study of Goiter. Characteristically, in his inaugural address before the American Medical Association, Dr. Lahey scorned to quibble or compromise. He took a firm stand and expressed his beliefs boldly. Speaking of his opinion that at that time the country was already committed to forceful opposition to Hitler he said: "I myself like it [the United States' position]. We have dared the dictator. It is too late to appease him, and the word has no meaning in his language. We should arrive at a conviction concerning isolation. Is it right? It is my conviction that it is not. I prefer destruction if it need be to survival in cowering terror. Give me positive commitment rather than compromising, unsatisfying safety."

The year 1940 marked a personal milestone for Dr. Lahey too—his sixtieth birthday. He was quite aware of some of its implications and in his quietly methodical way had a complete physical check-up before accepting the added responsibility of the presidency of the A.M.A. It was left to his staff and colleagues to celebrate the occasion in fitting fashion with an exceptionally successful surprise party at the Algonquin Club. Former fellows of the Lahey Clinic had assembled with their chief on the evening of May 30 for their regular alumni dinner. (June 1 is the actual birthday date.) On the floor below was an impressive gathering of the leaders in many fields of surgery and medicine. At dessert time they all came up, champagne glasses in hand, to offer toasts, sing congratulatory ditties, and admire the many-tiered birthday cake ornamented with such symbols of Dr. Lahey's hobbies as a miniature train, an airplane, and a pointer. Training his own hunting dogs and managing them in field trials had long been a favorite pastime. Twice he had won national championships in the amateur class, but like his hunting preserve in Alabama the dogs had to be abandoned in the heavy stress of wartime duties. Perhaps the patience was diverted from training dogs to teaching medical students! It is said that carving that elaborate confection was the one occasion on which Dr. Lahey was hesitant and timid with his knife! Certainly he was more visibly touched with emotion than ever in an operating room.

A more substantial memento derived from that sixtieth birthday party, viz., the Birthday Volume, a collection of studies by some sixty well-known doctors on their individual specialties or on matters influenced by Dr. Lahey. For example Dr. Cattell's piece on Lahey resection for cancer of the rectum, and Dr. Crile's discussion of the surgical treatment of essential hypertension. The book is fittingly dedicated:

> We of the medical profession, partakers of that fame which you have gained for us no less than for yourself, offer to you this birthday volume, in which you find yourself reflected more often than we intend to confess. You have honored medicine,

A moment of relaxation for Dr. Lahey—and some of his prize-winning hunting dogs.

and medicine delights to honor you. This is our birthday gift to you, our friend, advisor, and inspiration.

Those who work for him report in less flowery terms on that quality of inspiring others. "There are lots of ways of getting people to do their best for you. If they're efficient—and the doctor takes care to make good and sure they are—one of the best ways to keep 'em that way is to let them strictly alone. He can do that, and yet you always know when you come into the clinic whether he's here or not. He drops the spark, makes others move. After talking to him, people get enthusiastic and start to generate ideas on their own." And then, more reflectively: "He's the kind of man who, by the force and drive of his very nature would have accumulated money and prestige if he'd started out lacking it—which he didn't.

"He's fair too, hears your side promptly. His door's always open. The patients too learn very quickly that he's one of the easiest men at the clinic to see. That's because he sees everyone *now;* does everything *now;* he never postpones things or lets them pile up on his desk. And yet he probably gets through more work than anyone else. When he makes up his mind—and he makes it up quick too for he says he has a 50 per cent chance of being wrong—he acts fast and nothing stops him."

Along with his more forceful traits Dr. Lahey has a keen eye for detail. As one might guess from his own meticulous neatness, he dislikes sloppiness of all varieties among his associates and employees, whether evident in an unruly long bob, a couple of extra pounds around the hips, or unpolished dusty shoes. Concerning the latter he sent around a notice, accompanying it with cans of three shades of polish strategically disposed about the clinic.

Patients are held to the same austere standards. A placard in the entrance hall states clearly: "No smoking in the vestibule. There is a receptacle on the street corner for your cigarettes." And the memory of the hard straight chairs in the always crowded waiting rooms is ineradicable for anyone who has gone through the clinic. Those chairs, along with the absence of magazines to read, are an indication of Dr. Lahey's belief that sick people

like to talk to other sick people about their ailments. The doctor's courtesy is brisk and businesslike, but it is unfailing. And its essential human understanding is mirrored in the precepts inculcated into every clinic employee from receptionist to examining doctor. "Remember," says the chief, "the people who come here are sick—they deserve and should have special kindliness."

He's a good business man too. Always has the money in the bank before he builds, and then, liking the close association of a manageable group, jealously guards against overexpansion. He is capable of shrewd appraisal of Boston real estate values, a knowledge he gladly shares with any young clinic fellow faced with the necessity of providing living quarters for his family. Dr. Lahey's own home is but a few steps from the clinic, round the corner on Bay State Road. Thus he is spared any problem of commuting, and can literally use every moment to good advantage. His regimen, though frequently broken by speaking tours and lectures, is strict. The doctor is up by six, breakfasts with his wife at seven fifteen. At eight he starts operating, either at the Deaconess or New England Baptist Hospital. The clinic lacks operating facilities of its own. He lunches quietly at home, always finding a quarter or half hour for a relaxing nap. In the afternoon he sees patients and attends to other duties at the clinic until six. He dines at seven, and even should he be at a social function he is very apt to slip away for his usual ten o'clock bedtime. He neither smokes nor drinks —not that he holds convictions on the subject; merely that it is easier not to. A rigid routine, but one that keeps him fit for his strenuous life.

And so he goes about his manifold yet closely coordinated activities—a skillful and outstanding surgeon, but a great deal more than that; an originator of technics of operating and of bringing specialized, understanding medical care to thousands; an educator and directing force in medical training.

In the anniversary volume entitled *A History of the American Medical Association* celebrating a hundred years of service to the profession, Morris Fishbein evaluates phases of his contribution thus: "His chief literary contribution, in addition to many periodical articles, is the Lahey Clinic number of the Surgical Clinics of North America. [Annually he gets out the June issue.] He is a member of the editorial boards of *Surgery, Gynecology and Obstetrics,* and of the *New England Journal of Medicine.*

"His particular contribution to postgraduate education has been in the form of well-prepared lectures, always illustrated with slides and movies, delivered before medical societies, regional clinics, seminars, institutes and medical schools. He uses but few notes, and speaks entirely from his own experience, and the results obtained at the Lahey Clinic."

That estimate is inclusive and doubtless just, but it leaves out the warmth and sincerity of feeling felt for Dr. Lahey by those who have known him well, worked closely with him. Dr. Arthur Booth, past chairman of the Board of Trustees of the A.M.A., speaks for many when he says:

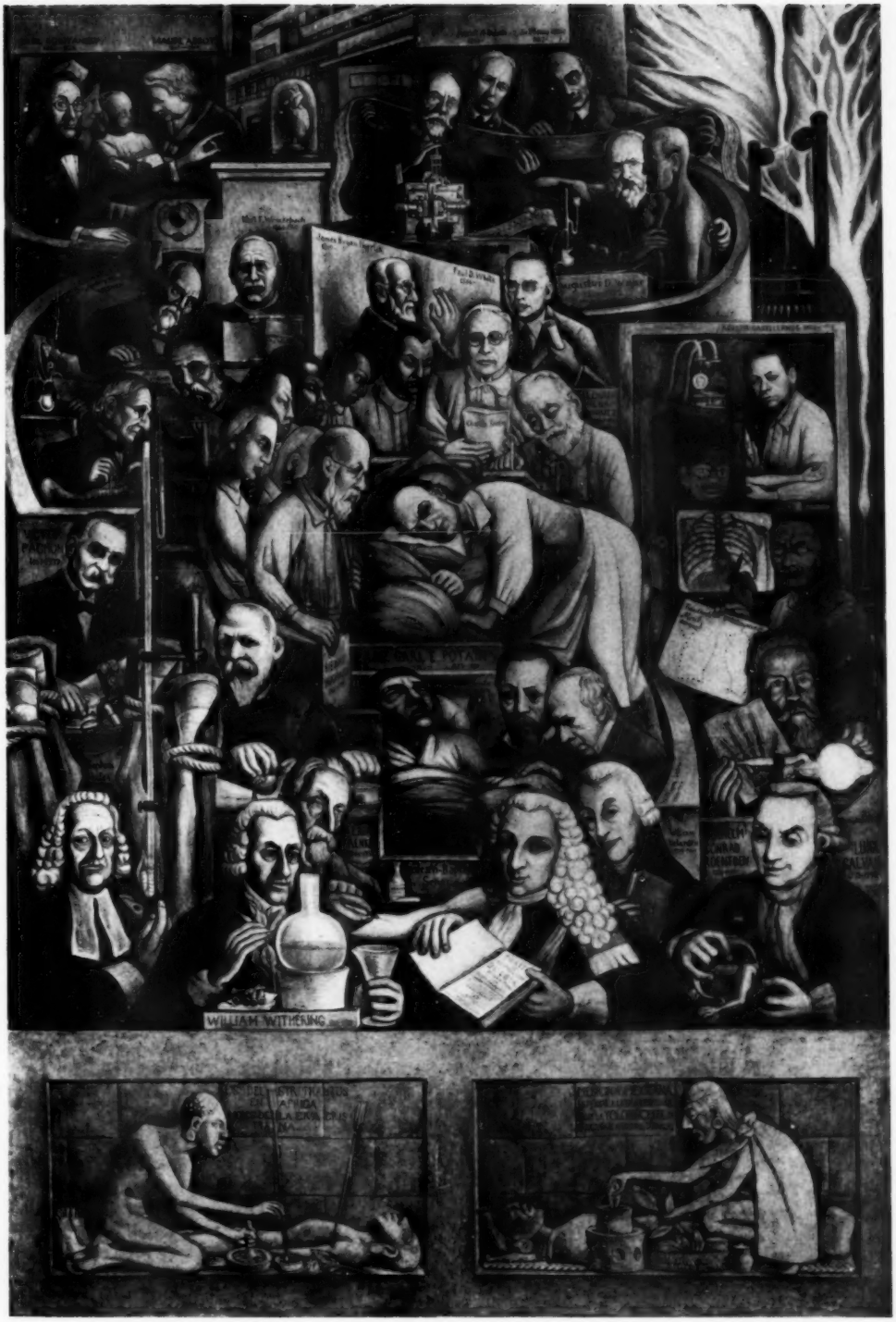
"That he has so many fond friends and enjoys such a broad acquaintance among doctors is due to his delightful personality, his approachableness and a willingness to give generously of his time and energy to his fellows. He has always found it difficult to decline an invitation to present scientific papers before medical societies or to serve in official capacities in medical organizations.

"I am particularly impressed that he accepts with such enthusiasm the broader responsibilities of his profession. To work within the close range of the doctor-patient relationship is obviously most essential and commendable, and by far too many very excellent men essay no further. Fortunately, it is given to some to look beyond the narrow confines of the consultation room or the clinic to that broader horizon where loom the vital problems of the advancement of medical science and art, especially in the field of supervision and direction of the Medical School and Hospital."

And a colleague who worked beside him in the tense war years sums it up even more tellingly.

"Dr. Lahey has said frequently, that 'he is devoting his life to the training of young physicians for better service in medicine and surgery,' and therein will be his noblest monument."

L. C. Deinard



A Portrait History of Cardiology

Murals by Diego Rivera, famed Mexican artist, reproduced by permission of the Instituto Nacional de Cardiologiá, Mexico City.

These reproductions, on paper suitable for framing, are available without charge to subscribers of Postgraduate Medicine. Address requests to IPMA Publishing Company, POSTGRADUATE MEDICINE, 516 Essex Building, Minneapolis 2, Minnesota.

EDITORIALS

AMERICAN SPECIALTY BOARD CERTIFICATION

It is quite consistent with the straightforward and somewhat aggressive policies of this relatively new journal, to discuss this subject and the controversy that is now brewing around it.

Specialty Board certification was seriously begun only about twenty years ago. Since that time, sixteen American Boards have established themselves as a profound influence on American medicine and its trends. All of these Boards started and have continued with two main avowed purposes, namely, to improve the standards of the practice of medicine in the various specialties, and to provide standards by which men qualified by actual training, experience, and ability, could be recognized as specialists.

There can be no question but that the Boards have been organized and conducted on a high plane; that medical politics have not entered into their functioning; that personal aggrandizement on the part of the Directors of the Boards cannot be charged in any degree; and that the leaders of the profession now conducting the affairs of the Boards are determined to keep them "clean." These men are entirely representative of the profession because they are appointed by the special national societies and academies which they represent, including the American College of Surgeons and the special sections of the American Medical Association. Their actions and rulings have been judicial and fair; in fact, no charge of unfairness toward candidates has ever been leveled at any Board. Nevertheless, the medical profession at large is becoming more and more critical of the American Boards and their certifications.

The Boards have been charged with setting up a "medical aristocracy" of specialists with which the general practitioner and the uncertified specialist are at a disadvantage. That this "aristocracy" has no barriers of race or color, its only card of admission being that of demonstrated ability, does not lessen the criticism.

It is charged that specialization and certification have been so overemphasized that all young doctors now aim to be specialists and too few want to be general practitioners, to the detriment of the public.

Discrimination has been alleged on the ground that many hospitals now require that anyone permitted to perform surgical work within them must be certified by an American Board, thus excluding the general practitioner who wants to do his own surgery. Going further, some hospitals have required that all staff appointments be restricted to American Board Diplomates. Another charge has been that older, though qualified, men who have not sought certification are being removed from their hospital staff positions and replaced by young men recently out of residencies but certified.

Some of these complaints have truth in them, others have only enough basis in fact to provide a complaint as an argument. Much of the criticism directed at the Boards has been unmerited.

In the first place, the Boards have accomplished for American medicine and the American public precisely what they set out to do. The standards of practice of medicine in this country have been vastly improved. The active educational program in the greatly expanded residency training system in American hospitals has bettered the training and practice of every

doctor exposed to it in a "residency approved" hospital, from interns up to and including the chiefs of staff. This is so regardless of whether they were working for some Board's certification, training for general practice, or in charge of and supervising the educational program. Everyone has profited, the patients most of all.

The Boards have succeeded in their aim to establish minimum standards of qualification, experience, and ability for men desiring to be recognized as specialists. It is no longer possible for a man to go away from home "for a postgraduate course" here or abroad and presently reappear as a full-fledged and unquestioned specialist.

No wonder some hospitals grasped at the chance to eliminate, by requiring certification for "courtesy privileges," some of those who "want to do their own surgery" regardless of lack of ability. What right has an untrained or poorly trained man to subject a patient to his surgery?

But the hospitals were wrong in making rulings requiring certification for staff appointments. The Boards disclaim any responsibility for such regulations, because they refute the fundamental principle of the Boards that Dispensary, Assistant, and Associate Staff hospital appointments provide an excellent training and proving-ground for young men. Many of these men might have been only partially trained by the residency system and logically seek to complete their Board's required credits by the preceptorship method under Assistant Staff appointments.

Senior Staff regulations having a reasonable degree of elasticity meet all criticisms. A simple rule in the "By-laws" of this writer's hospital staff should be quoted and more generally adopted to allow for the recognition and retention of acceptable, qualified men who have not been and never will be certified. "Members of the Senior Staff shall be required to be recognized specialists, and must be Diplomates of their respective specialty Boards, *except for outstanding reasons recognized by a three-quarter's vote of the Senior Medical Staff.*" Such a rule as this provides adequately for the general practitioner in the Department of Medicine, even on the Senior Staff, and certainly on the Associate or Assistant Staffs, where there should be ample place for general practitioners of ability. Even when hospitals, generally, establish formal Departments of General Practice this present regulation will need no alteration, because it is already so comprehensive.

Neither the general practitioner nor any other has valid reason to be antagonistic to these honest efforts toward improvement of the practice of medicine. Certification by a specialty Board is not another form of discrimination against anyone, nor is it the sole means of determining ability. It is, however, a thoroughly reliable yardstick by which the claim of specialist can now be measured.

P. T.

MEDICAL ASPECTS OF ANXIETY

It is well accepted by all of us that there is no sharp dividing line between the normal person and one who has an emotional illness. In all of us our adjustment varies from day to day. No one of us is ever a perfect success or a perfect failure. In many ways our adjustment can be symbolized by a pendulum which can be swayed from side to side by various factors or forces acting on it, but which returns to a central resting state when the force is removed. Some of us are thrown off balance more easily; others of us require greater stresses to disturb our equilibrium.

The tendency toward emotional illness is a *quantitative* thing: in some the tendency is small and the stress has to be great; in others where the tendency is greater, the stress can be less. All of us are constantly adjusting to conflicts and stress, and there is almost never a single cause in any emotional illness. At least four factors are always important in understanding any maladjustment; these factors are the previous experience of the individual, his own personality structure, his personality needs, and the environmental demands.

In such a complex and changing adjustment, it would not be unusual for inner conflicts to generate a feeling of inner tension which we sense consciously as anxiety. Indeed, it has been said that anxiety is the universal disease of our time, and that psychosomatic disease is the visceral expression of our anxiety. This view that anxiety is the predominant reaction in a functional illness is a valuable and unifying concept. In the various psychosomatic disorders, the symptom is due to a chronic and exaggerated state of the normal physiology of the emotion, with the feeling part repressed. Furthermore, chronic anxiety may produce long-continued visceral dysfunction which may in turn eventuate in structural changes of an organ.

We have now begun to formulate certain types of illnesses in which emotional factors play an important role. However, it is true that anxiety may affect any somatic function. Some of the more common manifestations of it are:

1. Gastrointestinal reactions.
   Peptic ulcer-like reaction, chronic gastritis, mucous colitis, hyperacidity, pylorospasm, etc.
2. Cardiovascular reactions.
   Paroxysmal tachycardia, pseudoangina pectoris, some types of hypertension, and neurocirculatory asthenia.
3. Genitourinary reactions.
   Dysuria, impotence, frigidity, some menstrual disturbances, etc.
4. Skin reactions.
   Some allergic responses (angioneurotic edema), factitia dermatitis, factor in certain eczematoid conditions.
5. Respiratory reactions.
   Asthma, nasal mucosal congestion, etc.

Man, thus, is an integrating organism maintaining a balance between the external and internal forces which determine his activities. When this balance is disturbed, disordered personality functioning and disordered body functioning results. Psychosomatic reactions are only the somatization of anxiety.

F. G. E.

INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION OF NORTH AMERICA

OFFICERS OF THE ASSOCIATION

PRESIDENT

Dr. Herman L. Kretschmer, Chicago, Ill.

PRESIDENT-ELECT

Dr. Evarts A. Graham, St. Louis, Mo.

PRESIDENTS OF CLINICS

Dr. John F. Erdmann, New York, N.Y.
Dr. Frank H. Lahey, Boston, Mass.

MANAGING DIRECTOR

Dr. Arthur G. Sullivan, Madison, Wis.

SECRETARY

Dr. Tom B. Throckmorton, Des Moines, Ia.

TREASURER AND DIRECTOR OF FOUNDATION FUND

Dr. Henry G. Langworthy, Dubuque, Ia.

SPEAKER OF THE ASSEMBLY

Dr. Mather Pfeiffenberger, Alton, Ill.

BOARD OF TRUSTEES

Dr. Edwin S. Hamilton, Kankakee, Ill.
Dr. Mather Pfeiffenberger, Alton, Ill.
Dr. Maurice R. Williamson, Alton, Ill.
Dr. Henry G. Langworthy, Dubuque, Ia.
Dr. John E. O'Keefe, Waterloo, Ia.
Dr. Tom B. Throckmorton, Des Moines, Ia.
Dr. John M. Dodd, Ashland, Wis.
Dr. Eugene S. Sullivan, Madison, Wis.

COMMITTEE ON MEDICAL RESEARCH AND ADVANCEMENT

Dr. Elliott P. Joslin, Boston, Mass.
Dr. W. Wayne Babcock, Philadelphia, Pa.
Dr. Charles H. Best, Toronto, Ont.
Dr. George Crile, Jr., Cleveland, Ohio
Dr. Evarts A. Graham, St. Louis, Mo.
Dr. Roy D. McClure, Detroit, Mich.
Dr. Jonathan C. Meakins, Montreal, Quebec
Dr. Eric Oldberg, Chicago, Ill.
Dr. James E. Paullin, Atlanta, Ga.
Dr. Erwin Schmidt, Madison, Wis.
Dr. Waltman Walters, Rochester, Minn.

PROGRAM COMMITTEE

Dr. Russell L. Cecil, New York, N.Y.
Dr. Henry A. Christian, Boston, Mass.
Dr. John R. Fraser, Montreal, Quebec
Dr. Duncan A. L. Graham, Toronto, Ont.
Dr. Herman L. Kretschmer, Chicago, Ill.
Dr. Frank H. Lahey, Boston, Mass.
Dr. Charles F. Martin, Montreal, Quebec
Dr. Charles W. Mayo, Rochester, Minn.
Dr. Howard C. Naffziger, San Francisco, Cal.
Dr. Charles H. Phifer, Chicago, Ill.
Dr. Leonard G. Rowntree, Miami, Fla.

New Drugs

Information published in this department has been supplied by the manufacturers of the products described.

PENICILLIN POTASSIUM TROCHES

PURPOSE: For intensive, topical penicillin therapy.

DESCRIPTION: Each troche contains penicillin 10,000 units, in a slowly dissolving, pleasantly-flavored base.

INDICATIONS FOR USE: Vincent's stomatitis, streptococcus pharyngitis, and tonsillitis.

DOSAGE AND ADMINISTRATION: Penicillin troches should be placed anywhere in the mouth, preferably into the buccogingival sulcus, and allowed to dissolve without chewing. One troche should be taken every one to four hours (depending on the severity of the infection) and just before retiring. If the patient awakens during the night another troche should be taken. With clinical improvement, dosage may be gradually reduced. As a general rule penicillin treatment is maintained until after the patient has been asymptomatic for at least forty-eight hours.

CAUTIONS: Topical use of penicillin may cause a contact dermatitis (urticaria, swelling, etc.) in hypersensitive individuals. In the mouth, hypersensitivity may be manifested by itching and swelling of the mucous membrane. With the occurrence of side effects the use of penicillin should preferably be discontinued. If continued administration is deemed necessary, the dose should be reduced to a minimum and great caution employed.

HOW SUPPLIED: Penicillin troches, 10,000 units, vials of 12 troches, boxes of 4 vials.

PRODUCER: Winthrop-Stearns, Inc., New York 13, N.Y.

DOLOPHINE

PURPOSE: Analgesic for relief of pain.

COMPOSITION: Heptanone derivative (4,4-diphenyl-6-dimethylamino-heptanone-3 hydrochloride) and an entirely different type of compound from either morphine or isonipecaine.

DESCRIPTION: A white crystalline substance, soluble in water and alcohol but insoluble in ether. It has a bitter taste and melts at 236° to 236.5° C.

INDICATIONS FOR USE: For control of pain and discomfort following surgery. Also used for alleviation of pain caused by ureteral stone; controlling pain due to metastatic lesions of malignant tumors and during treatment of pleuritic pains of pulmonary tuberculosis.

CAUTIONS: Nausea, vomiting, lightheadedness, drowsiness, dryness of the mouth, diaphoresis, and mental depression have occurred, but were not severe enough to necessitate stoppage of the drug. Not recommended for use alone as preanesthetic medication. Dolophine must be considered a potentially addicting drug and must be administered with caution similar to that attending the use of morphine until its status in general practice is established.

DOSAGE AND ADMINISTRATION: For moderate pain, 2.5 mg. of Dolophine given orally usually are effective for three to four hours. Severe pain may be controlled by oral dosage of 5 to 10 mg. Subcutaneous administration is not painful, and a somewhat more marked effect is obtained by hypodermic medication.

HOW SUPPLIED: Tablets Dolophine, 2.5 mg., 5 mg., and 7.5 mg., in bottles of 100 and 1,000. Ampules Dolophine, 10 mg. per cc., in individual 20-cc. rubber stoppered ampules. Syrup Dolophine, 10 mg. per 30 cc., in bottles of one pint and one gallon.

PRODUCER: Eli Lilly and Company, Indianapolis 6, Ind.

TABLETS ALUPEC

PURPOSE: Formula for quick and sustained antacid action.

COMPOSITION: Each tablet represents:

Aluminum hydroxide dried gel	10 gr.
Pectin	2½ gr.
Magnesium carbonate	1¼ gr.
Saccharin and aromatics	q.s.

One Alupec tablet will neutralize not less than 165 cc. of N/10 hydrochloric acid.

INDICATIONS FOR USE: Treatment of hyperacidity, including that accompanying peptic ulcer, as an aid to the promotion of healing and to control minor hemorrhage and relieve pain.

DOSAGE AND ADMINISTRATION: Adult, 1 tablet one-half to one hour after meals, repeated after two to four hours if indicated. Allow to disintegrate slowly in mouth, or crush or chew; follow with water or milk. When prescribed as an adjunct to ulcer treatment, dosage should be regulated by the physician.

HOW SUPPLIED: In bottles of 60 (6 to the box) and bottles of 500. Also available in liquid form.

PRODUCER: Pitman-Moore Company, Indianapolis 6, Ind.

URESTRIN

PURPOSE: For relief of menopausal symptoms.

COMPOSITION: The crystalline natural estrogens in this aqueous suspension are comprised of approximately 95 per cent estrone and 5 per cent estradiol, hippulin, and equilin. Prepared from estrogens obtained from urine of pregnant mares. Each cc. contains:

Estrogenic substances (20,000 International Units)	2 mg.
Physiological salt solution	q.s.

INDICATIONS FOR USE: For intramuscular use only, for administering estrogens suspended in water for relief of menopausal symptoms and for prolonging the period of relief.

DOSAGE AND ADMINISTRATION: The intramuscular injection of 2 to 4 mg. at intervals of one week will usually suffice, but more refractory cases may require more frequent administration.

HOW SUPPLIED: In 1 cc. vials.

PRODUCER: The Upjohn Company, Kalamazoo 99, Mich.

ABBOTT'S LIVER INJECTION, U.S.P.

PURPOSE: A parenteral solution of liver for intramuscular administration.

DESCRIPTION: Prepared from fresh liver by a uniform method designed to retain maximum amounts of the anti-anemia principle. It contains in concentrated form the Cohn liver fraction G. It is low in total solid content and high in hematopoietic activity. Injections are relatively non-irritating.

INDICATIONS FOR USE: Indicated for the treatment of the average uncomplicated case of pernicious anemia in relapse and for the maintenance of a normal blood picture.

DOSAGE AND ADMINISTRATION: Injection should be made intramuscularly. Least discomfort is experienced when the injection is made deep into the upper, outer quadrant of the gluteal muscle. Dosage requirements vary considerably according to the severity of the case. Each unit of Abbott's Liver Injection, U.S.P., represents the quantity of anti-pernicious anemia principle that will produce the clinical and hematopoietic responses defined as 1 U.S.P. unit (injectable) when given daily under controlled conditions to qualified patients with addisonian pernicious anemia.

HOW SUPPLIED: In three strengths: 15 units per cc., in 1-cc. ampules and 10-cc. vials; 10 units per cc., in 1½-cc. ampules, 10-cc. vials, and 30-cc. bottles; and 5 units per cc., in 10-cc. vials and 50-cc. bottles.

PRODUCER: Abbott Laboratories, North Chicago, Ill.

OBEX MULTIVITAMINS

PURPOSE: Treatment of general nutritional deficiencies.

COMPOSITION: Each capsule contains:

Bone meal Po. Purif	260 mgm.
Dibasic calcium phosphate	130 mgm.
Ferrous gluconate	65 mgm.
Vitamin A	5,000 I.U.
Vitamin D	1,000 I.U.
Thiamin HCl	5 mgm.
Riboflavin	3 mgm.
Pyridoxine HCl	2 mgm.
Calcium pantothenate	2 mgm.
Niacinamide	25 mgm.
Ascorbic acid	50 mgm.
Tochopherol (Equiv.)	3 mgm.
Inositol	10 mgm.
Folic acid	0.5 mgm.

INDICATIONS FOR USE: Prophylaxis therapy for expectant and nursing mothers; also, where general nutritional deficiencies exist in child and adult.

DOSAGE: 1 to 3 capsules daily as suggested by the physician.

HOW SUPPLIED: Bottles of 100 and 1,000 capsules.

PRODUCER: Ingram Laboratories, Inc., San Francisco, Cal.

TOMECTIN

PURPOSE: A palatable, nontoxic preparation designed for treatment of diarrhea of nonspecific origin as well as bacillary dysentery.

COMPOSITION: Each gm. contains:

Nickel pectinate	150 mg.
Sodium chloride	50 mg.
Together with all factors naturally present in dried fresh tomato pulp	800 mg.

DOSAGE AND ADMINISTRATION: Children and adults: 1 to 2 heaping tablespoonfuls (6 to 12 gm.) in water every two to three hours or after each bowel movement until recovery. Infants: 1 to 3 heaping teaspoonfuls every three hours or at each feeding.

HOW SUPPLIED: In wide-mouthed bottles each containing 50 gm.

PRODUCER: Ayerst, McKenna & Harrison, New York 16, N.Y.

DEXEDRINE SULFATE ELIXIR

PURPOSE: Central nervous stimulant.

COMPOSITION: The liquid dosage form of Dexedrine, each 5 cc. (1 teaspoonful) supplies the same amount of Dexedrine Sulfate (dextro-amphetamine sulfate, S.K.F.) as the standard 5 mg. tablet.

DESCRIPTION: The Elixir is the dosage form of choice in instances when it is desirable to produce the therapeutic effect of Dexedrine with greater speed than tablet medication allows.

INDICATIONS FOR USE: In depressive states, Dexedrine restores the patient's sense of well-being and capacity for work. The speed of action dispels as quickly as possible the characteristic "morning fatigue." In obesity, Dexedrine is established as the most effective drug for curbing appetite. It is also valuable in narcolepsy, postencephalitic parkinsonism, and alcoholism.

CAUTIONS: Contraindicated in agitated prepsychotic states, hyperexcitability, hypersensitivity to sympathomimetic compounds, and those cases of coronary or cardiovascular disease in which vasoconstrictors are contraindicated. Should be used with caution in cases with marked hypertension.

DOSAGE AND ADMINISTRATION: Depressive states—5 mg. to 10 mg. daily, one-half of the dose on arising, and the other half before noon. For control of appetite—15 mg. to 20 mg. daily, in 3 equal doses—before breakfast, at 11 A.M., and at 4 P.M.; or give largest dose at time of greatest hunger. Alcoholism—5 mg. to 15 mg. daily, one-half dose on arising, the other half before noon. Narcolepsy—10 mg. to 25 mg. daily, one-half of the dose on arising, the other half before noon.

HOW SUPPLIED: In 6 fluidounce bottles.

PRODUCER: Smith, Kline & French Laboratories, Philadelphia 5, Pa.

TIMOFAX

PURPOSE: Undecylenate ointment for the treatment of "athlete's foot."

COMPOSITION: Timofax contains undecylenic acid 10 per cent, as free acid and potassium undecylenate, in a scented, vanishing cream base.

INDICATIONS FOR USE: In acute and subacute dermatophytosis pedis ("athlete's foot"). In refractory, chronic cases, particularly those with established sensitivity to drastic chemical agents, a rest period followed by Timofax therapy may prove valuable.

HOW SUPPLIED: In ¾ ounce collapsible tubes.

PRODUCER: Burroughs Wellcome & Co., New York 17, N.Y.

PANSULFA

PURPOSE: Triple sulfonamide suspension for use in sulfonamide therapy.

COMPOSITION: Each 5 cc. teaspoonful contains 0.5 gm. (7½ gr.) combined sulfonamides.

DESCRIPTION: Liquid combining microcrystalline sulfathiazole, sulfadiazine, and sulfamerazine in 1:1:1 ratio.

INDICATIONS FOR USE: Pneumococcic, streptococcic, meningococcic, and staphylococcic infections, scarlet fever, rheumatic fever, erysipelas, otitis media, tonsillitis, urinary infections due to E. coli, Staphylococcus albus, Proteus and Pseudomonas.

DOSAGE: Adults—an initial dose of 8 teaspoonsful, followed by 2 teaspoonsful every 4 to 6 hours. Children—one teaspoonful for each 5 pounds of body weight per day, given in divided doses at four-hour intervals.

HOW SUPPLIED: 12-ounce bottles.

PRODUCER: The Wm. S. Merrell Company, Cincinnati, O.

FOLIX-B

PURPOSE: For treatment of anemia.

COMPOSITION:

Folic acid	3.3 mg.
Ferrous gluconate	300.0 mg.
Thiamin hydrochloride	3.0 mg.
Riboflavin	6.0 mg.
Niacinamide	30.0 mg.
Pyridoxine hydrochloride	0.1 mg.
Calcium pantothenate	1.0 mg.

DESCRIPTION: A new hematopoietic formula combining folic acid with iron and B vitamins.

DOSAGE: One tablet three times a day.

CAUTIONS: In pernicious anemia with neurologic signs, liver should be given.

HOW SUPPLIED: Bottles of 25 and 100 tablets.

PRODUCER: Cutter Laboratories, Berkeley 1, Cal.

CHLORGUANIDE HYDROCHLORIDE TABLETS

PURPOSE: Prophylaxis of malaria.

COMPOSITION: Chlorguanide is the shorter, nonproprietary name assigned by the Malaria Study Section of the National Institute of Health to N_1-*p*-chlorophenyl-N_5-isopropyl-biguanide. The hydrochloride of chlorguanide is a stable, white, crystalline powder, bitter-tasting and odorless, with a melting point of 240° C.

DESCRIPTION: Chlorguanide exerts a twofold effect as an antimalarial drug. It has a powerful action on the parasites in the red blood corpuscles, and it is one of the few antimalarial drugs that attack exoerythrocytic forms, and the only one that is active against these forms in more than one species. The potent action of the drug precludes the necessity of giving large doses. It does not stain the skin. It attacks both exoerythrocytic forms and blood forms of the malarial parasite. The gametocytes are attacked indirectly.

CAUTIONS: Occasionally nausea and vomiting have occurred from one-half to one hour after administration, but these minor symptoms were attributed to the disease rather than to the drug, and ceased with improvement of the clinical condition.

INDICATIONS FOR USE: In the treatment of both benign and malignant tertian malaria, chlorguanide inhibits development of the schizonts, and results in degeneration of asexual parasites before the formation of mature schizonts. Effective in clinical cure, radical cure, causal prophylaxis, and suppressive therapy in benign tertian malaria and malignant tertian malaria.

DOSAGE AND ADMINISTRATION:

Clinical cure of malignant or benign tertian malaria (suppression of acute attack)	0.1 gm. (1 tablet) 3 times daily for ten days
Radical cure of malignant tertian malaria	0.1 gm. 3 times daily for ten days, 0.1 gm. twice daily for fourteen days, or 0.2 or 0.3 gm. twice daily with a corresponding reduction of the treatment period
Radical cure of benign tertian malaria	0.1 gm. once a week, after the acute attack has been controlled
Causal prophylaxis of malignant tertian malaria	0.1 gm. (1 tablet) twice a week
Suppressive therapy of benign tertian malaria	0.1 gm. (1 tablet) twice a week or 0.3 gm. (3 tablets) once weekly

HOW SUPPLIED: In bottles of 100 and 1,000.

PRODUCER: Sharp & Dohme, Philadelphia 1, Pa.

ELIXIR LI-BETARON WITH FOLIC ACID

PURPOSE: For treatment of hypochromic anemia and as maintenance therapy in certain types of macrocytic or normocytic anemias.

COMPOSITION: Each 30 cc. (1 fluidounce) represents:

Ferrous gluconate (equivalent in elementary iron to 262 mg. per fluidounce)	2.27 gm. (35 gr.)
Folic acid	5 mg.
Thiamine hydrochloride	18 mg.
Riboflavin	6 mg.
Nicotinamide	60 mg.
Pyridoxine hydrochloride	2 mg.
Calcium pantothenate	5 mg.
Whole liver (as liver concentrate 1:20)	56.7 gm. (2 ounces)

(Total soluble constituents of 2 pounds of whole liver per pint of Li-Betaron with Folic Acid Elixir.) Also choline and other factors natural to liver.

DOSAGE AND ADMINISTRATION: Adults: A tablespoonful followed by water twice daily after meals. Children (6 to 12 yrs.): A teaspoonful followed by water three times daily after meals. Children (1 to 6 yrs.): A teaspoonful followed by water twice daily after meals. Infants (under 1 yr.): 20 drops from a standard dropper (10 minims) in milk four times daily.

HOW SUPPLIED: 8 fluidounce and one-half gallon bottles.

PRODUCER: Warren-Teed Products Co., Columbus 8, O.

Medicine Makes News

CUTTER LABORATORIES RESUME SHIPMENTS

ANNOUNCEMENT that Cutter Laboratories, Berkeley, California, are ready to resume shipment of Cutter solutions in Saftiflasks from its Berkeley and branch warehouses has been made by Fred A. Cutter, Vice President of the organization.

The full text of Mr. Cutter's statement is as follows:

"We are now ready to resume shipment of Cutter solution in Saftiflasks from our Berkeley and branch warehouses.

"We wish we could tell you that the cause of the contamination is now definitely known. We cannot truthfully do so. In the six weeks since we recalled our solutions, hundreds of thousands of flasks have been critically examined. Every piece of equipment and every instrument were meticulously checked. There was no evidence of equipment or instrument failure, and we could not definitely confirm closure failure or any other cause.

"We can assure you, however, that not a single bottle which was clear on visual inspection has been found to be contaminated, and that we will continue to do everything in our power to assure the safety that has been the cornerstone of our existence and growth for over fifty years."

A.P.M.A. MEDICAL SECTION BOARD ANNOUNCED

DR. THEODORE KLUMPP, President of the American Pharmaceutical Manufacturers' Association, has announced that the following ten physicians will serve as the Board of its recently created medical section:

Dr. Charles E. Dutchess, Schenley Laboratories, Inc. (Chairman); Dr. J. B. Rice, Winthrop-Stearns, Inc.; Dr. Stanton M. Hardy, Lederle Laboratories Division, American Cyanamid Co.; Dr. D. K. Kitchen, Bristol Laboratories; Dr. Paul C. Barton, Brewer & Company, Inc.; Dr. R. L. Conklin, Ames Company, Inc.; Dr. George Hazel, Abbott Laboratories; Dr. Irwin C. Winter, G. D. Searle & Company; Dr. Paul Spickard, Rexall Drug Company; and Dr. John M. Shaul, Maltbie Chemical Company.

SYMPOSIUM ON STEROID HORMONES

FINAL plans for the Symposium on Steroid Hormones to be held at the University of Wisconsin from September 6 through 8, 1948, have been announced by Dr. Edgar S. Gordon, Chairman of the Symposium Committee and Associate Professor of Medicine at the Medical School of the University of Wisconsin. This symposium is a part of the Centennial celebration of the Wisconsin State University. The final program includes the chemistry, metabolism, and biological effects of the steroid hormones, and the clinical applications of these substances will be discussed in detail.

This meeting is presented under the direction of the University of Wisconsin and the National Research Council Committee on Growth acting for the American Cancer Society. The Wisconsin Medical School, McArdle Memorial Laboratory for Cancer Research, and the Department of Biochemistry of the University have organized the program.

NEW GRANTS FOR VITAMIN STUDIES

NEW grants-in-aid, totalling $16,000, were awarded July 1 to scientists at four universities for vitamin research, according to an announcement by Robert S. Goodhart, M D., Scientific Director, The National Vitamin Foundation.

The new investigations involve eye health, the nutritional status of school children, the relationship between pyridoxine (vitamin B_6) and fat metabolism, and the effects of time elements on the utilization of water-soluble vitamins. The new grants bring to $126,320 the amount appropriated by the Foundation for nutrition research since March 1946.

Universities receiving the grants are Western Reserve University, School of Medicine, Cleveland, Ohio; University of Vermont, College of Medicine, Burlington, Vermont; Massachusetts Institute of Technology, Cambridge, Massachusetts; and the University of Southern California Medical School, Los Angeles, California.

Leaves from a Doctor's Diary

By Maurice Chideckel

July 1 . . . In his clinic today, gynecologist Allen was recounting the causes and cures of amenorrhea. For his clinical material he had Patricia Perkins who had not menstruated for three months. What didn't he mention? Ovarian dysfunction, atrophy of the endometrium, hypoplasia of the uterus, anorexia nervosa, disorders of metabolism, no estrin in the urine, and more and more causative factors. "This fine child of eighteen," he pointed to smiling Patricia, "is not married. Hence pregnancy is unthinkable." Utterly impossible. Who ever heard of an unmarried woman becoming pregnant? How could she? But "this fine child" called me this morning to tell that she has three hundred dollars cash. Would I please send her to a first class abortionist. How come?

* * *

July 2 . . . Several weeks ago Montgomery Boswell married for the second time. The bride told me that life without him would be an empty existence. Today I sent him to the hospital, as a dire emergency. "Madame," I told the wife, "your husband is not suffering from nervousness, and he does not need an operation, as you were told. He suffers from the bite of the female or widow spider, whose poison is fifteen times as strong as the poison of a rattlesnake. His life is to be despaired of. I fear he'll die." Her sister giggled. "When a female bites, she bites." Her bearded father shook his head approvingly. He turned to his married daughter. "Did he make you beneficiary of his policy?" he inquired with some anxiety. "Yes," said the wife. "Big policy?" father asked. "Forty thousand." Said the father, "Good." Said the sister: "Thank God. Come, I am hungry." And as all three walked off to lunch, the wife remarked: "I really would like him to live a little longer." What a noble soul. How devoted.

* * *

July 3 . . . So it is said: The reason a dog has many friends is because the animal wags its tail, instead of its tongue. Even excruciating pain, danger, and tragic events cannot stop this wagging that is sometimes destructive. And the Wise Man saith, life and death are within the power of the tongue. There sat in my office Mrs. Ayrest, suffering from causalgia, that painful state that arises from a focus of nerve irritability resulting from nerve damage. She is to enter the hospital for a sympathectomy. Her pain apparently ceased with the entrance of big Ralph Corrigan. "Shame on you," were the first words that greeted him. "I passed by your house yesterday afternoon. Disgraceful. If you must make love to your wife in that shameful way, why don't you at least pull down the blinds?"

Corrigan at first laughed. "The joke is on you, Mrs. Ayrest. Yesterday, I was not even home. I was out of town." Suddenly he awakened to consciousness, looked bewildered, then, in my consultation room he broke down and wept. I succeeded in prevailing upon Corrigan to believe me that she mistook him for another man. She did not.

* * *

July 6 . . . Instructor of philosophy Sinwell Claude is alert, eccentric and of vile temper. In addition to his other "gifts" he mistreats his French wife, beats cruelly his adopted son of ten, and proclaims aloud to his students the doctrine of white supremacy. He is plagued by a peptic ulcer, and I fail to see why he comes to consult me. His knowledge of psychosomatic medicine is something to marvel at. Each time he comes and he comes quite often, he never fails to discuss the correlation between frustrated desires and ulcer manifestations, the parasitic dependent desires arising from overindulgence in childhood and the development of symptoms when infantile cravings were denied. Today he entered smilingly. "I need your cooperation," he began. "No, not about my ulcer. I am organizing a national society. Not about the Negro. It's to be a society that will make all white men happy, and you are to be the national secretary of the American Society of Hedonism, the philosophy which makes pleasure the goal of life. The Greeks were right. The chief good of life is the enjoyment of personal pleasure in the gratification of desires. If it is our pleasure to eliminate a certain section of the population we shall do it. I think it's best that we call it by the modern name, Utilitarianism, which means to bring about the maximum pleasure of mankind. Are you with me? This organization will be our message to the ages." While he talked, he fingered a book of poetry that lay on my desk. I saw him tear out a page, and as he began to mutilate it I tore the end out of his hands.

It was probably William Cowper's "The Negro's Complaint." I only saved the last four lines:

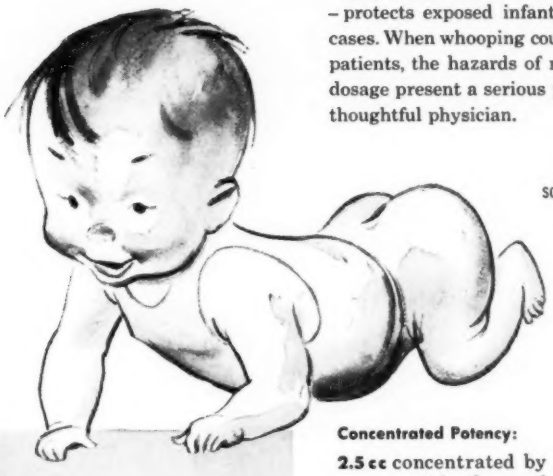
Fleecy locks and black complexion
Cannot forfeit Nature's claim;
Skins may differ, but affection
Dwells in white and black the same.

He fled when he saw Edna Buck coming in. Edna is a lady of the evening, and she comes weekly for a checkup. Her followers must be protected. Edna is no general practitioner. She specializes in married men. "He is one of my best customers," she meant the philosophy instructor. "It is not nice of you to betray confidence," I remonstrated with her. She laughed. "Don't these

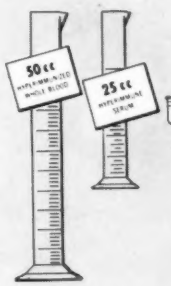
A thimbleful of dosage...

for a handful of baby . . . 2.5cc HYPERTUSSIS

concentrated human anti-pertussis globulin – protects exposed infants – treats critical cases. When whooping cough attacks small patients, the hazards of massive repeated dosage present a serious problem to every thoughtful physician.



2.5 cc Hypertussis provides the specific solution for therapy or passive prevention. The advantages are evident:



2.5cc HYPERTUSSIS

highly concentrated and purified gamma globulin of pooled human serum from healthy donors hyperimmunized with Super-Concentrate Phase I Pertussis Vaccine

The Specific Cutter Blood Fraction for Whooping Cough...

Concentrated Potency:

2.5 cc concentrated by fractionation to contain the antibody equivalent of 25 cc hyperimmune human serum.

2.5 cc delivers consistent gamma globulin potency in constant measured doses.

Small Volume Dosage:

2.5 cc concentrated gamma globulin reduces dosage volume 75%–minimizes injection trauma–permits repetition when required.

Homologous, sensitivity-free:

2.5 cc clear liquid homologous protein, Hypertussis is ready for intramuscular injection–avoids danger of reactions and serum sensitivity.

For 10-fold concentration in small volume dosage –specify ***CUTTER 2.5cc HYPERTUSSIS***
Anti-Pertussis Serum (Human)

CUTTER LABORATORIES • BERKELEY, CALIFORNIA

mugs betray the faith of their wives? Oh, it's such fun. When they don't come across and I tell them I'll talk it over with the missus, you should see them tremble. All their heads are just like door knobs. I can turn them on any side I want. It's a great life to be paid weekly by the weak. Look," and she displayed a big diamond necklace, and a mink coat. "Don't you think I am beautiful? They all fall."

* * *

July 10 . . . "Why was your daughter crying?" I asked Colleague Lightfoot. "Because," he told me, "the boy friend of hers did not kiss her once in six months. Last night, so she told me, thinking he was bashful she turned off the light. He rose to find out what's wrong with the lamp. She calls him a goof, and she does not want him." He sighed heavily. "How times have degenerated. I did not kiss Martha until we were married. I tell you, we are regressing. The marriages of today. Hmm. Fights, quarrels, and divorces. Medicine too. Shucks. When I practiced in the country, Dover's powder cured all, and so did calomel. Today. Nothing without lab, nothing without blood, urea, counts, x-rays and what have you. Well, what's the use."

What an example of the obsessive emotion of nostalgia, the cravings for the vanished yesterdays, the hastily gathered impressions that are wrong. To believe the medicine of bygone days superior to that of today, to ignore the strides of the healing art, the earth-shaking discoveries, man's conquest of the unknown—and from a medical practitioner. Maybe he still craves for the doctrine of laudable pus, of the Murphy button and of mercury by inunction. Did he forget the unnumbered victims of summer diarrhea, the death captaincy of pneumonia, the hospitals filled with typhoid cases, few of which survived?

Oh yes, about marriages. Quarrels and discords surely existed in generations past. Said Heine about a hundred years ago: "The music at a marriage procession reminds me of the music of soldiers entering a battle."

* * *

July 14 . . . There is Calvin Bradish who got me out of bed at 3 A.M because he was strangling, a chicken bone in his throat. "Twenty-five dollars if you get it out." I am no laryngologist, but I did extract the bone. Said he, "Did you take me seriously?" And what did I get? Nothing. Once, so I read, two sailors were drowning in midocean with no rescue in sight. "Lord," came from one sailor, "if I am saved I shall be faithful to my wife, never drink liquor, never cheat. . . ." "Stop lying," called the other sailor, "a ship is approaching."

Bradish, by the way, is a sort of an intellectual, and quite often quotes poetry. My secretary telephoned him about his not paying for a midnight call. "Because I don't pay you a little, don't pay another, and from the littles I accumulate a big sum. Remember Mackay's: A traveller on a dusty road strewed acorns on the lea; And one took root and sprouted up, and grew into a tree."

* * *

July 16 . . . Lawrence Sloan's acute coronary insufficiency cleared up but left a permanently damaged myocardium. The transient episodes of angina pectoris did not seem to impress him. Hence he continued to work by day and by night to accumulate more and more. "I have thirty thousand dollars," he told me, "twenty more and I stop." He stopped long before that.

July 19 . . . Margaret Randall. Beautiful Margaret with the madonna face and with the aura of saintliness that surrounded her. No, she could not think even of having a baby. How could she be bothered with a child, with all her social activities, her mah jongg and bridge organizations. She obtained some form of abortifacient paste and injected it into the uterine cavity. They buried her today and the games go on, and she is not even missed.

Sometime, somewhere in the long ago, I read the definition of a fool: "One who to his grave pursues the clouds he cannot own, and leaves a wealth of things undone, his grave a final stepping stone." And Chamfort said: "There are more fools than wise men, and even in the wise man himself there is more folly than wisdom."

Well, man will never conquer death, will never destroy the forces of corruption, will never slow man's mad rush for money and for power. For man acts by instinct and by impulse, seldom or never by reason and calculation. Perhaps it is better to be unaware of the coming of the inevitable, and in foolishness there is happiness, just as in ignorance and in the unknown Isn't knowledge painful at times?